

American Journal of Obstetrics and Gynecology

VOL. XX

ST. LOUIS, AUGUST, 1930

No. 2

Original Communications

CHORIOEPITHELIOMA

WITH ESPECIAL REFERENCE TO DISAPPEARANCE OF THE PRIMARY
UTERINE TUMOR

BY EMIL NOVAK, M.D., AND A. K. KOFF, M.D., BALTIMORE, MD.

*(From the Departments of Gynecology and Pathology, Johns Hopkins
Medical School)*

NO GROUP of tumors presents more interesting problems of pathologic diagnosis than do those arising from the chorionic epithelium. Some are obviously benign, others frankly malignant, but between these two extremes are other forms which it is difficult to evaluate from the standpoint of malignancy or nonmalignancy. Errors in diagnosis are perhaps more common in this field than in any other in gynecologic pathology.

There are several reasons for the difficulties in diagnosis presented by these tumors. Most important, perhaps, is the fact that the trophoblast is a normally invasive tissue. Even in normal pregnancy the uterine musculature is commonly invaded to a considerable depth, especially below the placental site, by chorionic wandering cells. Moreover, masses of trophoblastic tissue, and even clumps of chorionic villi, may be found in the veins of the uterine wall, or, for that matter, they may be deported to distant fields, more particularly the lungs. Schmorl's well-known studies¹ on this point indicate that such trophoblastic pulmonary emboli occur in at least 80 per cent of women during normal pregnancy. This capacity of normal trophoblast for what may be called physiologic metastasis, and its normal invasiveness, are

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

not very dissimilar from the well-known characteristics of cancer tissue, and help to increase the difficulties in the differential diagnosis of trophoblastic tumors.

Again, there is often comparatively little difference in the constituent elements of normal trophoblast, benign chorionic tumors, and the malignant chorioepitheliomas—certainly less than in the corresponding gradations of growths arising from other epithelial tissues. The diagnosis of malignancy must therefore take into consideration, perhaps more than elsewhere, such considerations as quantity of proliferative overgrowth, degree of invasiveness, etc. The factor of "capacity for independent growth," which Ewing so strongly stresses, is difficult to demonstrate by the microscope. Its biologic importance is obviously important, but its utilization in practical diagnosis is not clear.

In frankly malignant cases it is true that the constituent trophoblastic elements, more particularly those derived from the Langhans layer, show a more or less marked degree of anaplasia, with nuclear changes like those characterizing cancer cells in general. In the main, however, one is apt to derive less assistance from this criterion with chorionatous tumors than with most others.

It is easy to see, therefore, why mistakes in this particular field of pathologic diagnosis are so readily made, and the value of statistics collected from the literature must be discounted to this extent. When one considers that even normal placental remnants left in the uterus after miscarriage or full-term delivery have not infrequently led to the erroneous diagnosis of chorioepithelioma, one can understand differences of opinion in the interpretation of some of the more difficult pictures encountered.

Various attempts at the classification of the chorionic epithelial tumors have been made. The earliest of these, still not infrequently employed, was that proposed by Marchand² in 1895. This writer, whose classic work placed our knowledge of chorionic tumors upon a sound footing, recognized two main groups, a typical and an atypical. The first of these consists of tumors containing both types of trophoblastic tissue, the Langhans cells often predominating over the syncytium. The atypical variety, on the other hand, is composed of syncytium alone, and clinically it is characterized by a far lesser degree of malignancy.

One of the most pretentious efforts at classification is that of Ewing.³ This takes no cognizance of a benign group, although it is at least a question as to whether the benign hydatidiform mole should not be considered as a definite neoplasm. Many, of course, consider it a degenerative lesion, accenting particularly the hydropic changes in the villous stroma and the scantiness or disappearance of the villous blood vessels. But the trophoblastic proliferation is almost as con-

stant, and probably more characteristic. Individual villi in many hydatidiform moles often show little trophoblastic overgrowth, but this, in our experience, is often due to the fact that such villi are merely degenerated or regressive, because they are not in contiguity with the nutrient uterine wall. For that matter, they have often been cast off into the cavity of the uterus.

The study of hydatidiform mole in situ, so to speak, is apt to show a very different picture. Marked overgrowth of the trophoblast is commonly observed, so that it is easy to see how sections of such uteri could be mistaken for chorioepithelioma. For such reasons it is difficult to accept Ewing's view that "the differential diagnosis between a benign and a malignant hydatid mole usually presents no difficulty." This is especially true if one recognizes malignant mole as a definite entity, as Ewing does, giving it the name of chorioadenoma destruens. The wisdom of this is not clear, for the malignant mole metastasizes, recurs, infiltrates, and kills just as does the so-called chorioepithelioma, though not to the same degree. It is a malignant epithelial growth, and is better interpreted, it seems to us, as of carcinomatous nature, i.e., as a type of chorioepithelioma. The question involved is the same as that of the so-called "malignant adenoma," which, after all, is only a type or grade of adenocarcinoma, whether we label it malignant adenoma, Grade I adenocarcinoma, or what not.

The classification suggested by Ewing has not been accepted by gynecologists with any great enthusiasm; but, aside from such minor considerations as appropriateness of terms, we believe it to be in most respects a very sound one. We have already mentioned the fact that there is good reason to include the benign chorioma, i.e., the benign hydatidiform mole, in any scheme of classification of chorionic neoplasms. Mention, too, has already been made of the real difficulty which, in contrast to Ewing's view, is at times experienced in differentiating a perfectly benign mole—if one may judge from its clinical course—from his so-called "chorioadenoma destruens," if, as is often the case, the hydatidiform mole is characterized by marked trophoblastic proliferation with considerable penetration of the uterine musculature and vessels.

The aptness of the designation "chorioadenoma" appears unconvincing, in spite of Ewing's just contention that the villi possess many of the characteristics of glands. Morphologically, however, the villi themselves differ so much from glands, and the tumors arising from them have so little in common with adenomas as far as microscopic appearance is concerned, that the choice of the term "chorioadenoma destruens" for one group seems not such a happy one. Even the designation of "choriopapilloma," which Ewing mentions only to discard, would seem to be a better one. In other words, the function

of the parent tissue would seem a less logical basis for classification than the pathologic structure.

This, perhaps, is a less important question than that of whether this particular type of malignant chorioma should be divided as sharply as it has been by Ewing from the actual chorioepithelioma, even though its malignancy is definitely less. Would it not be better to class all the definitely malignant tumors as chorioepithelioma, and then to recognize the fact that, like other malignant epithelial tumors, various gradations of malignancy are encountered?

It is on such grounds as this that the view was urged by one of us (Novak)⁴ in a previous paper that the simplest division of these choriomatous tumors is into (1) chorioma benignum, corresponding to the benign hydatidiform mole; and (2) chorioma malignum or chorioepithelioma. The latter group, in other words, would include both the chorioadenoma destruens (the destructive placental mole) and the chorioepithelioma of Ewing. The subdivision into the two latter types is of value, just as is the subdivision of carcinomas in general into types and grades according to the degree of malignancy, so long as their fundamental unity is recognized.

As stated above, we do not believe that the differentiation of the benign from the malignant mole is always easy if one is dealing with sections of the uterine wall. In actual pathologic practice, of course, one is often helped immensely by the clinical history of the case. If a large mass of grape-like vesicles has been expelled or evacuated from the uterus, one is strongly inclined to interpret otherwise doubtful pictures as probably benign, because there is, in the malignant growths, a strong tendency to destruction of the villous pattern. This is, of course, far from an infallible criterion, but it has its value. As emphasized in Novak's previous paper, there is much reason to believe that many cases reported in the literature as chorioepithelioma have really been benign moles with abundant trophoblastic proliferation. After all, the differentiation must in some cases be based largely upon the amount of proliferation and the degree of invasiveness and destructiveness of a tissue which in itself may not differ so much, whether we are dealing with normal pregnancy, benign or malignant mole, or chorioepithelioma. When the trophoblast invades the uterine wall en masse, with extensive necrosis of the musculature, there is little doubt of malignancy. But when the villi are well preserved though perhaps gigantic, and necrosis and invasion not conspicuous, even extensive trophoblastic overgrowth is not in itself indicative of malignancy.

The third type of chorioma distinguished by Ewing, the "syneytioma and synectial endometritis" likewise will not commend itself to gynecologists as a clear-cut neoplastic entity, certainly in so far as "synectial endometritis" is concerned. The characteristics of the latter are those

commonly encountered in the inflammatory lesions following miscarriage or delivery. These are most often associated clinically with bleeding, and are produced by the retention of gestation products in the uterus. Villi are not infrequently found, but in addition there is often extensive infiltration of the uterine wall with syncytial cells. The picture, however, suggests an inflammatory process far more than a neoplastic one.

It is not the purpose of this paper to discuss the pathologic condition or the clinical characteristics of chorioepithelioma, but to call attention to one or two of the vagaries which distinguish it from other tumors. One of these, quite well known, is the fact that, while ordinarily it is an extremely malignant tumor, there are certain cases, approximately 10 per cent, which run a favorable course, with either spontaneous cure or cure after very incomplete operation. Another is the fact that in a rather considerable number of cases, in which extensive metastasis has occurred, no trace of the original tumor could be found. A third peculiarity is the fact that chorioepithelioma, as well as its benign prototype, is often associated with a rather characteristic group of changes in the ovaries. It is the second of these peculiarities with which we shall chiefly concern ourselves.

In 1902, Zagorjanski-Kissel⁵ collected nine cases of chorioepithelioma in which there was no primary tumor in the uterus. In eight of these there was a presumably primary tumor in the vaginal wall, and in one there were growths in the lungs and brain. A considerable number of these cases of so-called ectopic chorioepithelioma have been reported since then. De Zalka⁶ has recently collected a considerable group, and has added one of his own, in which there were tumor nodules in the left ovary, liver, lungs, and other organs, without a primary tumor in the uterus. The question at once arises as to whether such a primary origin in the uterus can be assumed, in view of the fact that chorioepitheliomatous growths have not infrequently been found entirely apart from pregnancy.

The first case of the latter type was reported by Kanthack and Eden⁷ in 1897. A considerable number of chorioepitheliomatous tumors of the male testis have of course been reported, and de Zalka was able to find in the literature some twenty-five cases of primary chorioepithelioma of the ovary, a much less frequent site. A rather questionable case of chorioepithelioma of the uterus, without preceding pregnancy, was reported by Lubarsch,⁸ while Bock⁹ has recorded an instance, which must also be regarded with skepticism, of a typical hydatidiform mole in a virgin twelve and a half years old.

Chorioepitheliomatous elements have not infrequently been found in dermoids in various locations (ovary, testis, anterior mediastinum, etc.), and Teacher,¹⁰ with considerable plausibility, believes that chorioepitheliomatous tumors found apart from pregnancy are teratomas "arising from some structure which has the morphologic value of an included ovum, and that the chorioepitheliomatous elements represent the actual trophoblast of the included ovum."

A case of the type reported by de Zalka, and representing the group with which we are now more directly concerned, was observed by Schmorl.¹¹ A primary vaginal tumor appeared eighteen weeks after a normal delivery. No evidence of involvement of the uterus, tubes, or ovaries was to be found. The patient died six months after her confinement, with metastases in the lungs, liver, intestines, and kidneys. In the

rather considerable series of cases of chorioepithelioma recently reported by Meyer,¹² Cases 7 and 8 are of this same type. In Case 7, in which a hydatidiform mole had been expelled, the patient was curetted for uterine bleeding some days later, on May 10. Bleeding reappeared at the middle of June, at which time a reddish-blue ulcerated nodule was excised from the anterior lip of the cervix. This proved to be a definite chorioepithelioma, so that hysterectomy was done. No trace, however, of hydatidiform mole or chorioepithelioma was found either in the curettings or in the uterus. The patient was well two and a half years after operation. Meyer interprets this case as probably one of ectopic chorioepithelioma, because the hysterectomy was done so soon after the expulsion of the mole, and yet no trace of chorioepithelioma was found in the uterus. This reasoning is, of course, not conclusive.

Case 8, in Meyer's series, was even more characteristic of this group. The patient expelled a hydatidiform mole on February 4, and was curetted on February 25 for bleeding. On February 27 bleeding occurred from a nodule in the vagina, and on March 2 the patient again entered the clinic. There was free bleeding from a friable nodule, about the size of a walnut, in the posterior fornix of the vagina. Histologic examination of this nodule showed chorioepithelioma. The patient died on March 19 of a streptococcus infection, present on admission. At the postmortem examination no trace of chorioepithelioma, either macroscopic or microscopic, could be found in the uterus, although a few scattered chorionic wandering cells were found in the uterine wall. Other cases of this general type have been reported by Krewer,¹³ Geist¹⁴ and others.

A case observed by Dr. Frank C. Marino, of Baltimore, who kindly turned the pathologic material over to us for study, was of this general type, though not so conclusive. About six months after an operation for pregnancy in a ruptured right tube, the patient was returned to the hospital, her condition suggesting a severe abdominal hemorrhage, presumably from a ruptured pregnant tube on the other side. The tube and the ovaries, both of which had been conserved at the first operation, were found to be normal. The blood filling the abdomen apparently had its source from numerous hemorrhagic growths scattered over the peritoneum. They varied in size from that of "a pea to that of a twenty-five cent piece," and were especially numerous over the ileum, omentum, and bladder. The hemorrhage from the intestinal implantations was so profuse that twelve inches of bowel had to be resected. In spite of blood transfusions the patient died after ten days, presumably because of progressive abdominal hemorrhage. The microscopic study of the implantations shows them to be typical chorioepitheliomas. Unfortunately the specimen of the original tubal gestation was no longer available for study, although it is said to have given no gross suggestion of malignancy.

Corresponding to the cases in which there has been a disappearance of a primary growth in the uterus, a group has been reported by various observers of corresponding disappearance of primary testicular tumors in the presence of extensive chorioepitheliomatous metastasis. A good illustration is furnished by the instance recently reported by Prym,¹⁵ whose patient at postmortem showed extensive metastases in the retroperitoneal glands, kidneys, lungs, liver, and elsewhere. No trace of active tumor tissue was found in the testis, although a cicatrized area marked its site, and the history indicated a definite tumor had been present. It will be noted that the distribution of metastases in these testicular cases is essentially the same as that associated with growths primary in the uterus.

The cases which have been mentioned, and which are based on careful microscopic studies, appear to establish the possibility of disappearance of the primary tumor as beyond reasonable doubt. A recent

case of our own, we believe, fortifies this assumption, especially as the original presence of the primary tumor was demonstrable in the curettage done some months before the patient died of extensive metastases.

CASE REPORT

The patient was a white woman, thirty-one years old, who was admitted to the hospital on November 13 with a history of headaches and increasing loss of vision for several months previously. She had had four children. There was nothing of note in her previous history until a few months before her admission to the hospital. Beginning in April, 1928, there had been slight bleeding about every two weeks. Normal menstruation occurred on June 16, lasting three days, and on July 13, when a curettage was performed at another hospital. Numerous small bits of tissue were brought away, although they did not, according to the report of the surgeon, suggest placental tissue. The pathologic report, after microscopic

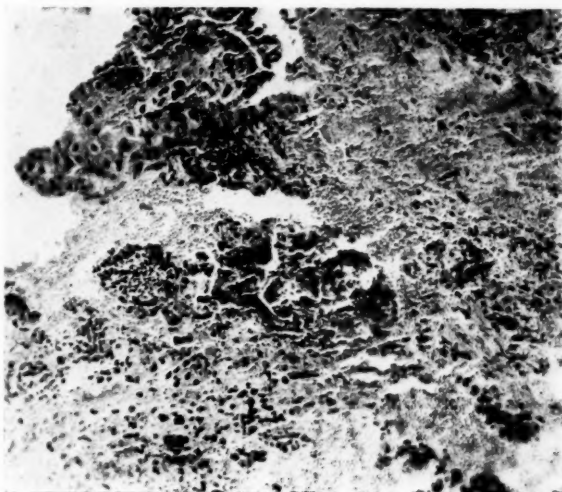


Fig. 1.—Curettings from case reported in paper, showing masses of trophoblastic tissue (both Langhans cells and syncytium), with no chorionic villi.

examination, was "Retained tissue following abortion." The slide upon which this diagnosis was based was kindly turned over to us, although the original curettings were not available. This slide will be discussed later.

The examination after admission to the Johns Hopkins Hospital showed bilateral choked discs, right homonymous hemianopsia and increased deep reflexes on the right side. Without going into details, a brain tumor was diagnosed, and operation done by Dr. Walter Dandy on November 17, a left occipital lobe tumor being removed. Death occurred on November 19. The tumor proved to be a typical chorioepitheliomatous metastasis.

The postmortem examination (Dr. Koff), in addition to the ragged cavity (about 10 cm.) in the left occipital lobe, from which the tumor had been removed, revealed also a number of chorioepitheliomatous nodules in the lungs and kidneys, as demonstrated by microscopic examination.

Special interest, of course, attaches to the findings in the generative organs. The uterus was of normal size. On opening it, the endometrium appeared somewhat congested, and at one point of the posterior wall, there was a small sessile

thickening which appeared more hemorrhagic than the remainder of the mucosa. There was a small amount of bloody discharge in the uterine cavity and also in the vaginal canal. The cervix was normal, except for a small erosion.

The left ovary was only slightly above normal size, and on section showed no abnormalities except a considerable number of tiny cysts, none larger than 1 cm. Some were filled with clear, and some with hemorrhagic fluid. The right ovary

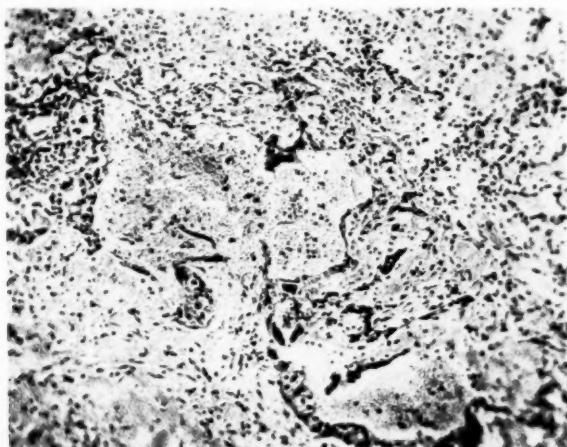


Fig. 2.—Section from lung metastasis, showing typical picture of chorioepithelioma.

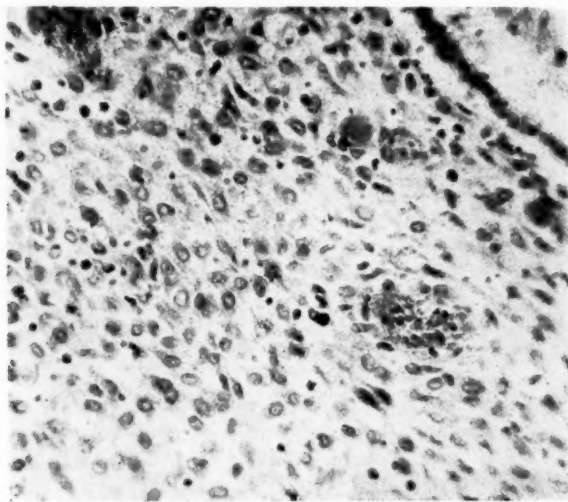


Fig. 3.—Section of endometrium, showing a persistence of decidua reaction in a few areas.

was about twice normal size, chiefly due to the presence of a thin-walled cyst measuring 2 cm. in diameter. Its wall was of greyish yellow hue, and the contained fluid was distinctly hemorrhagic. In addition this ovary contained a normal appearing corpus luteum, apparently in the stage of beginning retrogression, together with numerous small cysts similar to those found in the left ovary. The tubes were normal.

The microscopic examination of the tumor areas in the brain and lungs showed typical chorioepithelioma, with irregular masses of both syncytial and Langhans cells, much hemorrhage, and considerable coagulation necrosis.

Numerous sections made from the uterine wall failed to show any evidence of chorioepithelioma, or, indeed, of any trophoblastic tissue at all. There was much hemorrhagic infiltration of the uterine mucosa in the slightly raised hemorrhagic area described in the gross examination, and a moderate inflammatory infiltration was seen, but no villi or chorionic epithelium could be found. At some points there was still seen a definite decidual reaction in the stroma, but in most cases the stroma gave no suggestion of the preceding pregnancy. The persistence of this decidual reaction so long after the original pregnancy is of much interest. Certainly it would hardly be expected after the termination of a normal pregnancy, either by abortion or full-time labor. The natural assumption is that the persistence of this decidual reaction may be due to the fact that, although there is no trophoblast in the uterus, there is an abundance of this tissue in the metastases present in other organs, more particularly the brain and the lungs.

The microscopic study of the ovaries was of especial interest because it revealed a moderate degree of the multiple lutein cystic change so characteristically associated with chorioepithelioma or hydatidiform mole. Many of the small cysts shown on section of the ovary proved to be atretic follicles, most of which showed a complete absence of the granulosa, and no especial thecal change. A number of the smaller cysts, however, showed a striking lutein change in the theca interna. In addition to this, there was a larger cyst lined by a typical lutein layer, evidently of granulosal origin, together with a large, but regressive corpus luteum.

COMMENT

In cases of chorioepithelioma in which, in spite of extensive metastasis, the primary uterine growth appears to have disappeared, three possible explanations suggest themselves. In the first place, one might ask, especially in cases in which no definite history of pregnancy can be obtained, whether the uterus is actually the point of origin, and whether the distant growths are not really of teratomatous nature. As far as our own case is concerned, this view is untenable for various reasons, but chiefly because of the definite history of a recent pregnancy, and even more because the curettings at the original operation showed what was apparently a definite chorioepithelioma. (1)

Only one slide was available for study, and this showed only a few fragments of tissue. No villi were seen. The trophoblastic masses consisted of both syncytium and Langhans cells, and the latter especially presented such definitely malignant characteristics as mitoses, hyperchromatosis, etc. Certainly there can be little doubt of the diagnosis of chorioepithelioma, especially in view of the later history.

Generally speaking, the diagnosis of chorioepithelioma from curettings is a hazardous procedure, for reasons which are evident from the foregoing discussion. In certain cases, however, where large masses of trophoblastic tissue, without villi, are brought away by the curette, and where the microscope reveals unquestionable evidence of cell anaplasia, there is little possibility of error in the diagnosis of malignant chorioma. Even with smaller bits of tissue, as in our case, there would

be good reason for the diagnosis, although it is easy to see how malignancy could be overlooked in the ordinary routine examination. In our case, the diagnosis, as we have described, was made in the retrospect, i.e., after the death of the patient from metastases.

- 2) A second viewpoint which has been urged in the explanation of cases of the type we are discussing is that the chorioepitheliomatous growths in such distant organs as the lungs may arise from malignant degeneration of trophoblastic emboli even when the placenta itself shows no malignancy. This view is obviously rather difficult to establish, because of the difficulty of excluding small localized areas of chorioepithelioma in the placenta, for these can easily be overlooked or missed even on careful examination. Theoretically, there would seem to be no reason, however, why trophoblastic emboli carried to distant organs might not in some cases undergo malignant degeneration. In our own case, and for the reason already mentioned, this explanation would appear untenable.

- 3) The logical explanation of our own case would be that the uterine chorioepithelioma was the primary lesion, and that, although the metastases ultimately killed the patient, the primary lesion had disappeared. How great a part the curetting played in this, it is difficult to say. Most authors are inclined to doubt the possibility of removal of chorioepithelioma by the curette, because of the depth of involvement of the uterine wall, even in early stages. And yet, these tumors differ so much in their malignancy that it is hard to be dogmatic on this point. The unknown factor of local and general resistance must be considered, for certainly even complete recovery has occurred in not a few cases after very incomplete operation for chorioepithelioma of undoubted authenticity. For that matter, of course, even the possibility of spontaneous cure is admitted by all writers. In our own patient, moreover, the uterine lesion, at the time of the curetting, must have been quite early, for only a small amount of tissue was obtained and the uterine wall was described as being quite firm.

On the other hand, the fact remains that cases with otherwise similar courses have been observed in which no curetting was done, and that an analogous disappearance of a primary testicular tumor has often been observed with chorioepithelioma in the male. If it were possible to explain such occurrences, a great step would have been made in our study of tumors in general. Indeed, no tumor offers such inviting problems from this standpoint as does chorioepithelioma.

COMMENT ON OVARIAN CHANGES

As far back as 1898 Marchand called attention to the frequent association, with hydatidiform mole or chorioepithelioma, of multiple lutein cysts—or, as they were originally considered—multiple corpus luteum cysts. The frequency of this association is given variously by

different authors. Runge¹⁶ found such ovarian cystic changes in thirty-nine of sixty-three cases of hydatidiform mole, while others report a much lower incidence. These differences are partly explained by the fact that the ovarian changes vary greatly in degree, and that, in some instances, the ovaries show scarcely any microscopic enlargement, even though very characteristic changes are revealed by microscopic study. Unless the ovaries are actually removed at operation or postmortem, therefore, one is scarcely justified in assuming an absence of the characteristic changes even though careful bimanual examination shows no ovarian enlargement or tumor. The present-day prevalence of the conservative treatment of hydatidiform moles, therefore, does not lend itself to an accumulation of material for this sort of study.

Again, there can be little doubt that the incidence of this peculiar polycystic ovarian lesion depends a great deal upon the age or duration of the hydatidiform mole or chorioepithelioma, as urged by Schröder. It is quite possible, indeed, very probable, that at some time or other, and to some degree or other, this lesion occurs constantly in the course of either benign or malignant chorionatous disease. A number of authors, for example, are inclined to the belief that large cysts develop only after expulsion of the mole, but this view, supported though it seems to be by a number of observations, is not universally accepted.

The size of the ovarian tumors, as already mentioned, is very variable. In some cases they may be as large as a man's head, in others the ovaries show little or no gross enlargement. The same variation is seen in the size of the individual cysts.

The two questions which have excited most discussion with reference to these tumors, are (1) their significance in relation to the intra-uterine disease; and (2) the origin of the lutein cells lining the cysts. Both of these questions will be discussed in a later paper by the present authors, based upon a somewhat larger amount of material. There can be little doubt that the ovarian lesion is secondary to the chorionic disease, and not, as many have believed, vice versa. The study of the present case, moreover, suggests that the abnormal trophoblastic overgrowth in the uterus may excite lutein-like transformation in both granulosa and theca interna. For example, in some follicles the granulosa is intact and shows no lutein transformation, while the thecal cells have undergone marked lutein cell metaplasia. The thecal origin of lutein cells is again indicated by the occurrence of masses of lutein cells deep in the walls of atretic follicles and even of old corpora fibrosa. On the other hand, one may find definite lutein strata, which, from their position and relation to other structures, such as the so-called "glashaut," certainly suggest a granulosal origin. This whole question, however, together with a review of the literature, will be reserved for another paper.

SUMMARY

After a discussion of the classification of choriomatous tumors, this paper is devoted to a consideration of the disappearance of the primary uterine tumor in cases of chorioepithelioma. A case is reported in which such a disappearance was noted, although the patient later died of extensive metastases in the brain and lungs. That there was an original primary tumor in the uterus was proved by examination of the uterine curettings several months before the patient's death. Autopsy showed no trace of chorionic tissue in the uterus. Other cases of this type which have been reported are reviewed, and the various explanations discussed. The autopsy showed the ovaries to be the seat of characteristic hyperlutein changes, and gave an opportunity of studying the histology of the pituitary body in relation to these changes. The discussion of these ovarian and pituitary changes is reserved for a second paper.

REFERENCES

- (1) *Schmorl*: Verhandl. d. deutsch. path. Gesellsch. 8: 39, 1904. (2) *Marchand*: Monatschr. f. Geburtsh. u. Gynäk. 1: 419, 513, 1895; Ztschr. f. Geburtsh. u. Gynäk. 39: 173, 1898; Ztschr. f. Geburtsh. u. Gynäk. 32: 405, 1895. (3) *Ewing*: Surg. Gynec. Obst. 10: 366, 1910. (4) *Novak*: J. A. M. A. 78: 1771, 1922. (5) *Zagorjanski-Kissel*: Arch. f. Gynäk. 67: 326, 1902. (6) *De Zalka*: Am. J. Path. 4: 59, 1928. (7) *Kanthack, and Eden*: Trans. Lond. Obst. Soc. 38: 71, 1896. (8) *Lubarsch*: Arbeiten a. d. path. Inst. zu Posen, 1901, p. 230. (9) *Bock*: Inaug. Diss. Köln, 1923. Abstracted in Zentralbl. f. Gynäk. 48: 169, 1924. (10) *Teacher*: J. Obst. & Gynec. Brit. Emp. 4: 1, 1903. (11) *Schmorl*: Quoted by Zagorjanski-Kissel, q. v. (12) *Meyer*: Ztschr. f. Geburtsh. u. Gynäk. 92: 259, 1927-1928. (13) *Krewer*: Ztschr. f. Geburtsh. u. Gynäk. 48: 66, 1903. (14) *Geist*: Surg. Gynec. Obst. 32: 427, 1921. (15) *Prym*: Virchow's Arch. 265: 239, 1927. (16) *Runge*: Arch. f. Gynäk. 69: 33, 1903.

26 EAST PRESTON STREET.

Rickman, J.: On the Etiology of Prolapse of the Uterus. J. Obst. & Gynec. Brit. Emp. 36: 70, 1929.

The author attempts to correlate the various factors entering into the etiology of prolapse, by using a formula capable of universal application in medicine, i.e.

A predisposing factor: Constitutional.

A specific factor: Increased intrapelvic pressure.

Contributory factors: Including a variety of phenomena themselves requiring subdivision and classification.

Inciting Causes: For example, a fall.

He favors this formula because it coordinates factors not previously linked, adds a notion of quantity to the factors contributing to the etiology, and lays more stress on defects of function than on anatomy.

FRANK SPIELMAN.

THE BLOOD-PLATELETS IN PREGNANCY AND IN THE PUERPERIUM

BY P. BROOKE BLAND, M.D., ARTHUR FIRST, M.D., AND
LEOPOLD GOLDSTEIN, M.D., PHILADELPHIA, PA.

(From the Department of Obstetrics of the Jefferson Medical College)

IN SEVERAL recent papers^{1, 2, 3} dealing with the morphology of the blood in pregnant women, it was shown that a moderate to a severe grade of secondary anemia and a rapid sedimentation rate are usually present. The deficiency of the blood is early overcome after labor without special treatment, and the sedimentation rate returns to normal within two to six months after delivery.

In a further study of the blood in pregnancy, we have made determinations of the number of platelets (thrombocytes) in pregnancy and in the puerperium. This investigation was undertaken because comparatively little is known of the behavior of the platelets in pregnancy, and because of the important relation these elements are thought to bear to blood clotting. It was hoped that this study would throw some light on the coagulability of the blood in pregnant women.

It is definitely known that the process of coagulation is dependent on three essential elements: the blood-platelets, fibrinogen, and calcium salts. Modern theories in general agree that fibrin is formed by the action of thrombin on fibrinogen. Intravascular clotting does not occur because thrombin exists only in its inactive form of prothrombin. Morawitz (1904)⁴ believes that in shed blood a coagulating agent is liberated by the disintegration of the blood-platelets and by the extravascular tissues which in the presence of calcium salts converts prothrombin into active thrombin.

It has been pointed out by several investigators^{5, 6} that a pronounced increase in fibrinogen occurs in pregnancy. Greisheimer⁷ working in conjunction with others has recently pointed out a correlation existing between the fibrin content of the blood and sedimentation, namely: that as the fibrin content increases, the sedimentation rate becomes more rapid. The excessive production of fibrinogen is probably an expression on the part of the body to control hemorrhage during labor by increasing the elements necessary for hastening blood coagulation.

Investigations of the calcium content of the blood in the gravid state have recently been reported in the literature. DeWesselow,⁸ Krebs and Briggs,⁹ Bogert and Plass,¹⁰ and Kehrer,¹¹ found the content lessened in the latter half of pregnancy. Meigs, Blatherwick and Cary¹² could find no significant lowering of the calcium in the whole blood or in the serum of pregnant cows. Denis and King,¹³ taking 9 to 11 mg. per c.c. as a standard for normal serum calcium, discovered significant changes in pregnant women.

Hueper¹⁴ found experimentally in dogs that the increased calcium content of the blood produced by injections of parathyroid extract augments the coagulability of the blood and favors the formation of thrombi.

From the results of the studies of these investigators, it is obvious that any increased coagulability of the blood encountered in pregnancy cannot be attributed to a hypercalcemia, and that the calcium content of the nongravid state is usually sufficient for the proper coagulation of the blood during labor.

The existence of blood-platelets has been known since 1882 when Bizzozero¹⁵ isolated the platelets and described their morphology. Numerous hypotheses have been suggested for their histogenesis. On morphologic grounds, Wright¹⁶ claimed that platelets are detached particles of the cytoplasm of the giant cells of the bone marrow (megakaryocytes) which are thrown into the blood stream.

The blood-platelet determinations for the normal as reported by various authors are indicated in Table I. The marked variations noted are due in part to the use of different methods of examination and to the fact that the number of platelets is altered by various physiologic states and changes from day to day.^{17, 18}

REVIEW OF THE LITERATURE

Our knowledge concerning the number of blood-platelets in different pathologic conditions, as well as in pregnancy, is incomplete, owing largely to different methods of enumeration. Only a few meager studies have been made of the variations of these bodies in pregnancy and in the puerperium.

TABLE I. NORMAL PLATELET COUNTS

AUTHOR	NUMBER OF PLATELETS PER C.M.M.
Thomsen ²⁷	250,000-300,000
Wright and Kinnicutt ¹⁶	226,000-367,000
Hayem*	250,000
Zeller*	500,000-750,000
Emden*	200,000-300,000

*Quoted from Gram.⁶

Bizzozero¹⁵ was the first to contend that the platelets increased in pregnancy.

Rebaudi¹⁹ claimed that the number of platelets at any period of gestation is always greater than normal (300,000 per c.mm.), though it is subject to very noticeable fluctuations. He noted an increase during the first, second, and third months with a maximum of 630,000 per c.mm. in the first half of the fourth month. The total number declined slowly and gradually during the fifth and first half of the sixth month, reaching the maximum average of 950,000 per c.mm. at term, and a maximum average of 1,500,000 per c.mm. in the last stage of labor. Rebaudi observed a rapid diminution in the number of platelets within twenty-four hours after delivery, these falling to a minimum average of 560,000 per c.mm. He found an increase on the third day which continues during the fourth and fifth days until a maximum average of 930,000 per c.mm. is reached. After this peak is obtained, the number decreases in the following week until by the twelfth day of the puerperium it falls to an average of 670,000 per c.mm.

Dawborn, Earlam, and Evans²⁰ studied the blood-platelets in 28 unselected cases of parturition and 5 cases of cesarean section. They observed that these bodies

began to multiply in number on the fourth day postpartum, reaching a maximum representing a 100 per cent increase on the tenth to twelfth day. The platelets then gradually diminished in number, the counts made after three weeks being approximately normal. In two cases of severe hemorrhage the curves slightly exceeded the average. In 6 patients the rise was insignificant, whereas in 14 others the count was doubled or more than doubled. In 5 cases of cesarean section, the average rise was approximately 200 per cent, while the lowest was 146 per cent. The count reached a maximum in from nine to thirteen days and fell rather more slowly than in the normal parturition series.

Louros²¹ examined the blood of 66 women and found that platelets in the same individual varied from time to time. In 15 young nonpregnant women, he found an average of 350,000 platelets, ranging from 250,000 to 500,000 per c.mm. In 10 cases of pregnancy in the second month, he noted counts ranging from 370,000 to 600,000. In one case of parturition with fever, 420,000 platelets were present. In 14 gravid women in the eighth month, the count ranged from 500,000 to 650,000.

TECHNIC OF PLATELET COUNTING

The direct method of counting blood-platelets was employed in this study. By this method the blood is mixed according to the ordinary hemocytometric principle, using a diluting fluid which fixes and stains the platelets.

The diluting fluid of Rees and Ecker was found altogether satisfactory for our purpose as it affords one the opportunity of counting the red cells at the same time.²² The technic is essentially simple.

The diluting fluid is drawn to near the 1 mark in the ordinary pipette used for counting red blood corpuscles. Blood from a freely bleeding puncture is then drawn exactly to the 0.5 mark, and finally the diluting fluid is again drawn to the 101 mark. This gives a blood dilution of 1 in 200. In order that clumping of the platelets may be avoided, special care must be taken to draw the blood into the pipette immediately after puncture. The Levy-Hausser counting chamber is filled and ten minutes allowed for the platelets to settle to the bottom of the chamber before counting.

The platelets appear as sharply outlined, round, or oval glistening bodies.

The diluting fluid consists of:

Sodium citrate—3.8 per cent aqueous solution	100.0 c.c.
Formaldehyde—40 per cent	0.2 c.c.
Brilliant cresyl blue	0.1 gm.

With a dilution of 1 to 200, the platelets are counted in 400 small squares, and the number multiplied by 2,000. Thus, if 120 platelets are enumerated in 400 squares, the count would be 240,000 for each cubic millimeter.

The platelet determinations in this study were made under the direct supervision of Dr. Baxter L. Crawford, Pathologist of the Jefferson Medical College Hospital.

TABLE II. BLOOD-PLATELET DETERMINATIONS IN 50 NONPREGNANT WOMEN

THOUSANDS PER C.MM.	NUMBER OF PATIENTS	PERCENTAGE
150-200	3	6
201-250	13	26
251-300	15	30
301-350	12	24
351-400	4	8
401-450	3	6
Total	50	100

Table II indicates the results of blood-platelet determinations in 50 nonpregnant women made according to the method herewith described. Dr. Crawford believes that a variation of 50,000 in the count is of no significance and may be due either to unavoidable error in enumeration, or to some alteration in the physiologic state of the patient examined. This adds to the difficulty of properly evaluating the rise or fall in the platelet count in any condition studied.

It is seen from Table II that 40 (80 per cent) of the 50 nonpregnant women examined had counts varying from 200,000 to 350,000 per c.mm.

PLATELET DETERMINATIONS IN PREGNANCY

The platelets have been studied in 230 gravid women and in 100 of these further studies were made during the puerperium. The counts were made on all patients registering in the Antenatal Clinic of the Jefferson Medical College Hospital. The results of the examinations in the 230 patients at different periods of gestation are described in Table III. Complete data disclose that 177 (77 per cent) had from

TABLE III. BLOOD-PLATELET DETERMINATIONS IN PREGNANCY

THOUSANDS OF PLATELETS PER C.M.M.	NUMBER OF PATIENTS	PERCENTAGE
150 to 200	11	4.8
201 to 250	50	21.7
251 to 300	64	27.8
301 to 350	63	27.4
351 to 400	20	8.7
401 to 450	12	5.2
451 to 500	6	2.6
Over 500	4	1.8
Total	230	100.0

200,000 to 350,000 platelets per c.mm., whereas 42 (18.2 per cent), had over 350,000 platelets per c.mm. No noteworthy relation between the platelet count and the length of gestation was found. A comparison of the platelet count in the nonpregnant and pregnant individual (Tables II and III) reveals that the number of platelets is not appreciably altered in pregnancy.

The average level of platelets is apparently not influenced by the diminished number of erythrocytes, nor by the rapid sedimentation rate ordinarily occurring in pregnancy.

PLATELET DETERMINATIONS IN THE PUERPERIUM

Platelet determinations of 100 unselected patients were performed within twenty-four hours after labor, on the third to fourth day, and on the eighth to the tenth day of the puerperium. The results of these examinations are depicted in Tables IV, V, and VI and in Fig. 1.

In this study only variations of more than 50,000 platelets were considered of importance. A count which did not vary by 50,000 in either direction during the puerperium was considered as "unchanged."

Table IV lists the counts of 100 women made within twenty-four hours after delivery. In this table it is noted that 27 per cent of the patients gained over 50,000 platelets per c.mm. Included in this group are 9 women with an increase of over 100,000 per c.mm.

Table V indicates the counts made three to five days after delivery. This table reveals that 55 women gained more than 50,000 platelets within five days after labor. Of this number, 20 gained between 50,000 and 100,000 whereas 35 gained over 100,000.

TABLE IV. PLATELET COUNTS WITHIN TWENTY-FOUR HOURS AFTER DELIVERY

THOUSANDS PER C.MM.	NUMBER OF PATIENTS	UN- CHANGED*	REDUCED OVER 50,000	INCREASED 50-100,000	INCREASED 100-200,000	INCREASED OVER 200,000
150-200	1	0	0	1	0	0
201-250	26	18	0	3	4	1
251-300	26	21	0	5	0	0
301-350	32	17	3	9	3	0
351-400	5	3	1	0	0	1
401-450	6	2	4	0	0	0
451-500	1	0	1	0	0	0
Over 500	3	0	3	0	0	0
Total	100	61	12	18	7	2
Percentage		73				27

*Increase or Reduction Less than 50,000.

TABLE V. PLATELET COUNTS THREE TO FIVE DAYS AFTER DELIVERY

THOUSANDS PER C.MM.	NUMBER OF PATIENTS	UN- CHANGED	REDUCED OVER 50,000	INCREASED 50-100,000	INCREASED 100-200,000	INCREASED OVER 200,000
150-200	1	0	0	0	1	0
201-250	26	2	0	7	11	6
251-300	26	12	0	8	5	1
301-350	32	15	5	4	7	1
351-400	5	2	0	0	2	1
401-450	6	3	2	1	0	0
451-500	1	1	0	0	0	0
Over 500	3	0	3	0	0	0
Total	100	35	10	20	26	9
Percentage		45				55

TABLE VI. PLATELET COUNTS EIGHT TO TEN DAYS AFTER DELIVERY

THOUSANDS PER C.MM.	NUMBER OF PATIENTS	UN- CHANGED	REDUCED OVER 50,000	INCREASED 50-100,000	INCREASED 100-200,000	INCREASED OVER 200,000
150-200	1	1	0	0	0	0
201-250	26	5	0	7	12	2
251-300	26	9	3	4	9	1
301-350	32	6	5	3	5	3
351-400	5	0	0	4	1	0
401-450	6	5	1	0	0	0
451-500	1	1	0	0	0	0
Over 500	3	1	2	0	0	0
Total	100	38	11	18	27	6
Percentage		49				51

Table VI lists the counts of the same group of women within eight to ten days after delivery. It is observed that 51 per cent of the group had a gain over 50,000. Of these 51 women, 18 gained 50,000 to 100,000, 27 gained 100,000 to 200,000, while only 6 gained over 200,000 per c.mm.

It is particularly noted that no patient with a count of over 400,000 per c.mm. showed a gain in the puerperium.

A comparison of the alterations in the platelet count in the course of the puerperium is shown in Fig. 1. This reveals that 18 to 20 per cent of the patients had a rise of 50,000 to 100,000 during the various stages of the puerperium. Only 9 per cent, however, had the large increase

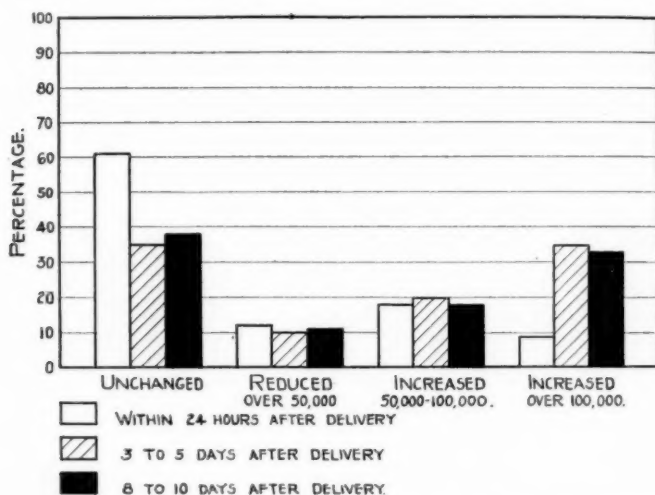


Fig. 1.—Variations in blood-platelet count of 100 patients in puerperium.

of over 100,000 within twenty-four hours, whereas 33 to 35 per cent showed this excessive increase within three to ten days after childbirth. The gain of over 100,000 represents in many cases a rise of 30 to 100 per cent above the original count in pregnancy.

DISCUSSION

From the results of our study it is apparent that no marked variation in the number of blood-platelets occurs in pregnancy. The significance of the failure of the blood-platelets to increase in pregnancy remains undetermined. It seems, however, that a rise in the platelets is not essential in increasing the blood coagulability in pregnancy. The added power of the blood to clot in pregnancy may be explained entirely on the basis of an increased fibrinogen content of the blood. A low platelet count encountered in pregnancy, however, may be an indication of the presence of a hemorrhagic diathesis, especially when the deficiency in platelets is associated with a severe grade of anemia. In such a contingency it may be of value to stimulate platelet forma-

tion by the use of the ultraviolet light or by irradiation with small doses of either radium or the roentgen ray as suggested recently by Cramer and Bannerman.^{23, 24}

Factors Concerned in the Platelet Rise in the Puerperium.—It is difficult to render an exact explanation of the rise of the platelet count in the third to the tenth day of the puerperium. According to Dawborn, Earlam and Evans, it appears that hemorrhage as ordinarily encountered is not the dominant factor, but that the destruction of tissue and its subsequent absorption may be the cause of the elevation.

It may be that the increased formation of platelets is in the nature of a defensive act of the body against infection, analogous to the physiologic leucocytosis in gestation. Evidence that the thromboeytosis is a defensive mechanism is found in the work of Téoumine.²⁵ This investigator believes a low platelet count in the puerperium is indicative of poor resistance on the part of the patient. The fluctuation in the number of platelets in puerperal infection probably reflects the relationship between the defensive forces of the organism and the aggressive forces of the infection. In cases of puerperal sepsis ending in recovery, Téoumine found the number of platelets was much higher than in those ending fatally. Nine of 11 fatal cases of puerperal septicemia had counts below 200,000 per c.mm., and toward the end the counts decreased still further. A gross increase in the number of platelets may probably be regarded as a favorable prognostic sign, while a continuous fall may signify a failure of the defensive forces of the body and possibly point to a fatal determination.

There were no puerperal infections or other serious complications in our series of 100 patients, so that we are unable to correlate the platelet fluctuations with any pathologic condition of the patient. It is our belief, however, that the platelet rise is a reaction of the body against invasion by pathogenic organisms.

It has been recently suggested that a relationship exists between the number of platelets and thrombosis. It was observed by Dawborn, Earlam and Evans²⁰ that the tendency to thrombosis increases when the platelets are augmented in number. These authors suggest that with a retarded flow of blood, thrombosis is more likely to occur in blood rich in, rather than poor in, platelets. In 2 cases, high platelet counts were found in association with thrombosis. The underlying cause of the slow regular swing of the thromboeytes appearing so regularly after operation and parturition could not be determined. They conclude that this late rise of platelets is a natural phenomenon—a physiologic response on the part of the bone marrow—comparable to the early leucocytosis which occurs in pregnancy.

Dawborn cites the following interesting case: A woman, para ii, aged thirty-three, was anemic before delivery. On the morning of the tenth day, postpartum, examination showed 1,270,000 platelets.

On the night of the tenth day she developed a thrombosis of the left internal saphenous vein, extending to the middle of the leg. On the following day examination showed 540,000 platelets. The count continued to fall for the next few days. On the twenty-second day, a rise was again noticed, and on the twenty-third day, the clot extended to the femoral vein in the groin. The platelet count continued to rise until the forty-sixth day, when the patient left the hospital much improved.

A similar case was reported by Evans²⁶ who observed a high platelet count in a patient with splenic anemia who died of mesenteric thrombosis.

No definite conclusion can be reached regarding the relation of thrombocytosis (increased number of platelets) to thrombosis or phlebitis. Further clinical and pathologic studies may enlighten us regarding this connection.

SUMMARY AND CONCLUSIONS

1. The blood-platelet count for the nonpregnant woman was found to vary from 200,000 to 350,000 per c.mm.
2. Platelet determinations were made in 230 women in various stages of gestation, and in 100 of these after delivery.
3. It was found that 177 (77 per cent) of the 230 gravid women had from 200,000 to 350,000 platelets per c.mm. of blood, while 42 (18.2 per cent) gave a count of over 350,000. Therefore, it may be stated that the blood platelets are not appreciably increased in pregnancy.
4. Twenty-seven per cent of the 100 women gained over 50,000 platelets per c.mm. within twenty-four hours after labor, whereas 63 per cent had either a gain of less than 50,000 platelets or had a lower count than in pregnancy.
5. Counts made three to five days after delivery reveal that 55 women (55 per cent) gained more than 50,000 platelets. Of this number, 35 gained over 100,000 platelets.
6. Fifty-one per cent of the counts made on the group of 100 women eight to ten days after delivery showed a gain of over 50,000. Twenty-seven of these 51 women gained 100,000 to 200,000, whereas 6 gained over 200,000 per c.mm.
7. The cause of the rapid rise in the number of the platelets in the puerperium is undetermined. It has been suggested that the multiplication of platelets may be physiologic, a natural response of the body to safeguard against possible infection. Further investigation is necessary to ascertain the reason for the postpartum increase in the platelets and to determine if any relation exists between the increase and the occasional occurrence of thrombophlebitis in the lying-in period.

REFERENCES

- (1) Bland, P. B. and Goldstein, L.: *J. A. M. A.* 93: 582, 583, 1929. (2) Bland, P. B., Goldstein, L., and First, A.: *Am. J. M. Sc.* 179: 48-66, 1930. (3) Bland, P. B., Goldstein, L., and First, A.: *Surg. Gynec. Obst.* 50: 429-434, 1930. (4)

Morawitz, P.: Deutsche Arch. f. Klin. Med. 79: 215-233, 1904. (5) Bruchsalter, S.: Zentralbl. f. Gynäk. 51: 2010-2014, 1927. (6) Gram, H. C.: Acta Med. Scandinav. 54: 1-16, 1920. (7) Greisheimer, E. M., Johnson, O. H., and Ryan, Mary: Am. J. M. Sc. 177: 816-827, 1929. (8) DeWesselow, O. L. V.: Lancet 2: 227, 228, 1922. (9) Krebs, O. S., and Briggs, A. P.: AM. J. OBST. & GYNEC. 5: 67-72, 1923. (10) Bogert, L. J., and Plass, E. D.: J. Biol. Chem. 56: 297-307, 1923. (11) Kehler, E.: Arch. f. Gynäk. 112: 487-523, 1920. (12) Meigs, E. B., Blatherwick, N. R., and Cary, C. A.: J. Biol. Chem. 37: 1-75, 1919. (13) Denis, W., and King, E. L.: AM. J. OBST. & GYNEC. 7: 253-258, 1924. (14) Hueper, W.: Arch. Path. 3: 14-25, 1927. (15) Bizzozero, J.: Vireh. Arch. 110: 261-332, 1882. (16) Wright, J. H., and Kinnicutt, R. S.: J. A. M. A. 56: 1457-1459, 1911. (17) Als, Emil: Acta Med. Scandinav. Suppl. No. 7, 263-268, 1924. (18) Pratt, J. H.: J. Med. Research 5: 120-126, 1903. (19) Rebaudi, S.: Am. Jour. Obst. 56: 475-481, 1907. (20) Dawborn, R. Y., Earlam, F., and Evans, W. H.: J. Path. & Bact. 31: 833-873, 1928. (21) Louros, N. C.: Arch. f. Gynäk. 119: 110-114, 1928. (22) Todd, J. C.: Clinical Diagnosis, Philadelphia, 1927, W. B. Saunders Company, p. 748. (23) Cramer, W., and Bannerman, R. G.: Lancet 216: 992-994, 1929. (24) Cramer, W., and Bannerman, R. G.: Lancet 216: 1048-1050, 1929. (25) Téoumine, S.: Gynéc. et Obst. 15: 436-463, 1927. (26) Evans, W. H.: J. Path. & Bact. 31: 815-832, 1928. (27) Thomsen, O.: Acta Med. Scandinav. 53: 507, 1920.

1621 SPRUCE STREET.

1703 SPRUCE STREET.

1717 PINE STREET.

Lee, Y. C.: The First Menses of Korean Girl Students. China M. J. 44: 1, 1930.

The average age of the first menses of 424 Korean girl students is fifteen years and this is very much earlier than that of girls in the northwestern part of Korea and Chinese women, but later than that of Japanese women.

Classified by occupation, the daughters of farmers, educators, and religionists develop later.

The first menses occur most often in the spring and summer. This agrees with Taguchi and others.

C. O. MALAND.

Weinberger, R.: Association of Grippe and Menstrual Disturbances. Med. Klin. 24: 1794, 1928.

During the course of an epidemic of grippe the author observed menstrual disturbances apparently due to the grippe. The patients usually had herpetiform vesicles on the upper lip, nose, and tip of the tongue, and about two-thirds of them had a skin affliction which resembled impetigo contagiosa. The temperature was seldom high. The patients, who before their illness menstruated normally, began to have hemorrhages, accompanied by pain as soon as the grippe started. The hemorrhages usually lasted four to six days. Physical examination both general and local showed no cause for this bleeding other than the grippe. The menstrual condition was regarded as being toxic in origin.

J. P. GREENHILL.

THE RESULTS OF AN INVESTIGATION AND THE TREATMENT OF STREPTOCOCCAL PUERPERAL SEPSIS AT THE TORONTO GENERAL HOSPITAL*

By W. A. DAFOE, M.B., TORONTO, ONT.

(Fellow in Obstetrics & Gynaecology, University of Toronto)

THE high maternal mortality rate in this country is a subject of great concern, not only to the medical profession, but also to the laymen. A conservative conclusion obtained from the statistical reports of maternity clinics in different parts of the world shows puerperal sepsis to be the cause of 30 per cent of the deaths following childbirth. These reports also show that the organism found in the blood stream in from 70 to 90 per cent of the fatal cases is the *Streptococcus hemolyticus*.

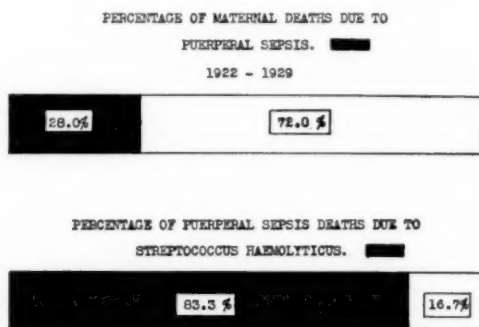


Fig. 1.

The investigation here reported was carried on over a period of two years (from the end of January, 1927 until the beginning of January, 1929) in the Burnside Department of the Toronto General Hospital, under the direction of Professor Hendry. We hoped to obtain information about the hemolytic streptococci which would be of practical value in either decreasing the incidence of that organism, or in treating cases already infected. It was thought necessary to find out the incidence of hemolytic streptococci in the cervical canal during:

1. The latter weeks of pregnancy.
2. The end of labor.
3. The puerperium in normal and all morbid cases.

Before this work was begun, a plan was outlined for the investigation of all cases of puerperal sepsis and for the classification and treat-

*Read at a meeting of the Academy of Medicine, Toronto, January 23, 1930.

ment of those cases due to the *Streptococcus hemolyticus*. Accurate results of this plan were kept and will be reported later in this paper.

Prenatal cultures from the cervical canal were obtained from our clinic patients about two weeks before the expected date of labor. During labor the cultures were taken either at the beginning or during the middle of the second stage. This procedure was carried out after the patient had been prepared. The vaginal orifice was spread open with the gloved fingers and a swab stick was inserted between the presenting part and the cervical or vaginal wall. The third group of birth canal cultures were taken from a certain number of patients with a normal puerperium, as well as from every patient showing a temperature of 100° F. for twenty-four hours. In the normal cases the cultures were taken on various days, from the second to the tenth. But in those cases showing a temperature, as indicated, the cultures were taken immediately. The postpartum cultures were taken under rigid aseptic precautions by exposure of the cervix with a speculum.

The culture material in each of these cases was obtained by rotating the swab stick in the cervical canal or around the presenting part. These sticks were then replaced in the sterile test tubes and taken to the bacteriologic laboratory. There the material to be examined was gently stroked across the surface of a sterile blood agar plate. These plates were then placed in the incubator and left for twenty-four hours. At the same time, a direct smear was also made and stained in the routine way by Gram's method, which often showed the presence of streptococci in chains, and thus enabled us to start the special treatment immediately. The blood agar plates were examined the following day after planting the cultures. The colonies of *Streptococcus hemolyticus* were distinguished by their size and shape and by the characteristic surrounding hemolytic zone. As we were particularly interested in the presence or absence of the *Streptococcus hemolyticus*, a record of the other organisms was not kept. It was necessary at times to transplant doubtful colonies into glucose broth which would be incubated for twenty-four or forty-eight hours and the fluid examined by direct smear.

To a clinician, the classifications of streptococci appears to be very complicated. We made no attempt to differentiate the types of hemolytic streptococci and followed a simple, general division suggested by Schottmüller. He divides streptococci into three groups, i.e.:

1. *Streptococcus hemolyticus*
2. *Streptococcus anhemolyticus*
3. *Streptococcus viridans*

The division is based on their cultural characteristics on blood agar. The hemolytic streptococcus is by far the largest group of the streptococci. This is found in many cases of infection and particularly in those found in the ear, nose, and throat. In puerperal sepsis we have an unlimited number of strains of *Streptococcus hemolyticus*. These varieties apparently all produce an exotoxin, and there is similarity in the reactions of these exotoxins as tested by the intracutaneous injections. Our series of 100 cases, three years ago, tested out with three varieties of puerperal sepsis exotoxin, showed that from 22 to 33 per cent of the patients were susceptible to this toxin, but only 2.85 per cent were susceptible to the scarlet fever toxin.

The appearance of genital erysipelas and scarlet fever in the puerperium may only be incidental, but some close association between the organisms producing puerperal sepsis, and those producing other infections, is within the realm of reason. This problem remains to be definitely proved. Possibly environment influences these organisms to a great extent.

The results of the cervical cultures were as follows:

1. *Antenatal Cultures*.—Five hundred eleven patients had cultures taken before labor during the various months of the two years. Only 7 of these cultures were positive for hemolytic streptococci.

2. *Labor Cultures*.—Cultures were taken from 432 patients during delivery and 14 were positive for hemolytic streptococcus. Out of these 14 cases, the *Streptococcus hemolyticus* disappeared during the puerperium in 7 but remained to produce definite evidence of infection in the other 7.

3. *Postpartum Cultures*.—In the third group, 435 patients were examined, 515 cultures taken and the *Streptococcus hemolyticus* was found in 52 cases. Of these 32 were cases of puerperal sepsis and the remaining 20 cases showed no evidence of infection.

The total number of cultures was 1458.

The total number of patients was 1378.

It was found in this investigation that the *Streptococcus hemolyticus*, although present, was not a common inhabitant of the cervical canal

TABLE I. CERVICAL CULTURES POSITIVE FOR STREPTOCOCCUS HEMOLYTICUS, BURNSIDE DIVISION, TORONTO GENERAL HOSPITAL

MONTH	ANTENATAL	NATAL	POSTNATAL	CASES OF PUERPERAL SEPSIS
<i>1927</i>				
February	1	0	5	1
March	1	1	2	2
April	0	1	6	5
May	0	0	8	4
June	1	0	3	3
July	0	0	1	0
August	0	0	1	1
September	1	0	0	1
October	0	0	0	0
November	0	0	0	0
December	0	0	1	0
<i>1928</i>				
January	0	1	1	1
February	0	5	7	4
March	0	0	3	3
April	2	2	6	2
May	1	1	2	1
June	0	0	0	0
July	0	0	1	1
August	0	3	2	2
September	0	0	2	1
October	0	0	0	0
November	0	0	1	0
December	0	0	0	0
Total	7	14	52	32

during pregnancy. This group of organisms was found in 3.24 per cent and 10 per cent of the cases in which cervical cultures were taken during labor and the puerperium. These organisms were much more

TABLE II. CERVICAL CULTURES POSITIVE FOR STREPTOCOCCUS HEMOLYTICUS, 1927-1928. BURNSIDE, TORONTO GENERAL HOSPITAL

ANTENATAL			NATAL			POSTNATAL			TOTAL
SMEARS	+ VE	PER CENT	SMEARS	+ VE	PER CENT	SMEARS	+ VE	PER CENT	SMEARS
497	7	1.4	432	14	3.2	529	52	9.8	1458

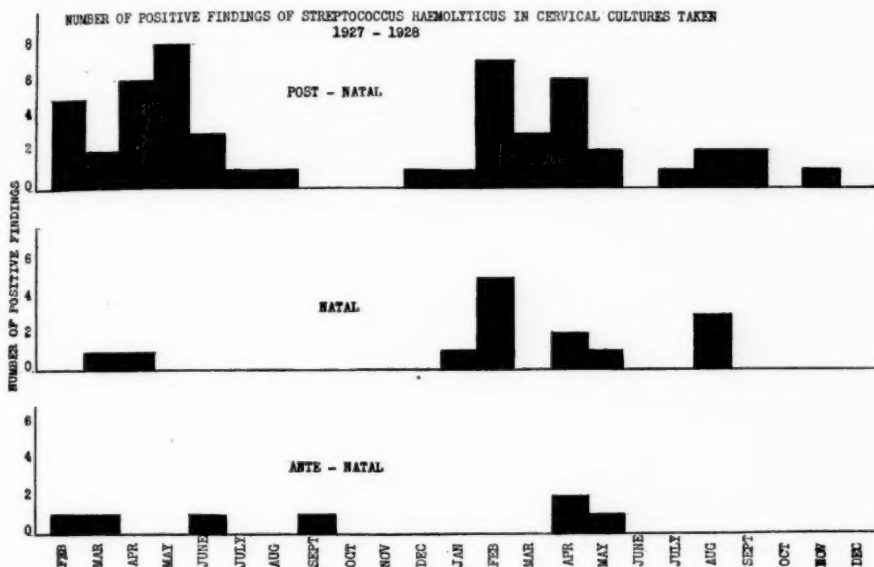


Fig. 2.

frequently found during the months of February, March, April, and May, both in the cultures taken at labor and also in those taken during the puerperium.

- (a) 52 positive smears during the puerperium over a period of two years.
- (75 per cent) 39 positive smears during months of February, March, April, and May.
- (b) 14 positive smears during labor over a period of two years.
- (71 per cent) 10 positive smears during February, March, April, and May.

During these two years, our records show infections of all types to be the cause of 32 per cent of the total morbidity (100° F. for twenty-four hours after the first day). Also, that over half of all the infections were cases of puerperal sepsis due to *Streptococcus hemolyticus*. The morbidity rate was found to be higher in the winter and early spring

months and this finding coincided with, and was dependent upon the increased evidence of the *Streptococcus hemolyticus* in the cervical canal during these months.

The study of the relationship that exists between *Streptococcus hemolyticus* and puerperal sepsis should include not only a summary of the incidence of this organism in the genital tract during pregnancy and the puerperium, but also a survey of the clinical manifestations and the results of treatment in this type of infection. We therefore kept over the same period (1927 and 1928) a record of the treatment carried out for all those patients showing a positive cervical swab for *Streptococcus hemolyticus*.

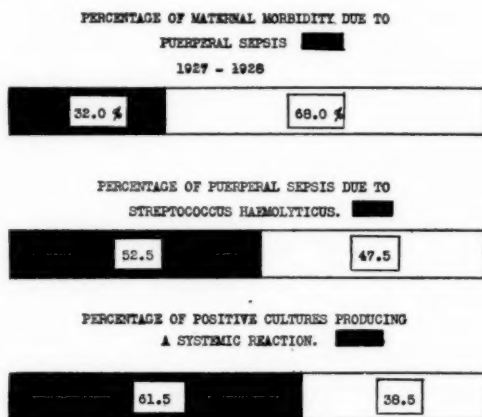


Fig. 3.

In order to find the cause of morbidity in the puerperium, it was necessary to investigate every case showing a temperature of 100° F. for twenty-four hours, as carefully as possible. This investigation included:

1. A careful examination of all systems, i.e., respiratory, gastrointestinal, cardiovascular, genitourinary, etc., and the breasts.
2. Blood examination: (a) R.B.C.
(b) W.B.C.
(c) Hemoglobin estimation.
(d) Blood culture if necessary.
3. Cervical culture.
4. Urine examination: (a) Routine.
(b) Microscopic.
(c) Culture.

Those cases of puerperal sepsis showing a positive cervical swab for hemolytic streptococci were divided into three groups with a subdivision into two for the third group. This division was based upon the patient's general and systemic reaction as evidenced by the height of the temperature. It was noted in the severe cases of infection that

the pulse curve was comparatively much higher than is usual in other types of infection. Another consistent finding in serious cases was the scantiness of the uterine discharge which maintained a characteristic chocolate colored serous appearance.

As mentioned previously, there were 32 cases of puerperal sepsis due to *Streptococcus hemolyticus* and 20 cases where the streptococcus found, produced no reaction. The grouping of these cases was as follows:

Group I: Serious cases, a positive cervical smear for streptococcus hemolyticus and a temperature over 102° F. for twenty-four hours.

Group II: A positive cervical smear and a temperature of 101° to 102° F. for twenty-four hours.

Group III: (a) A positive cervical smear and a temperature of 100° to 101° F. for twenty-four hours. (b) Positive cervical smear and no elevation of temperature.

Treatment.—The prophylactic measures of treatment were included in the antenatal care and the careful technic of the delivery room. The other measures carried out were based upon the division of the cases into the three groups already mentioned and were as follows:

Group I:

(Over 102° F. for twenty-four hours.)

- a. General Measures:
 1. Isolation.
 2. Fowler's position.
 3. Heat to abdomen.
 4. Ergot and quinine.
 5. Fluids pushed by mouth, or intravenously.
 6. Special care of perineum.
 7. Sunshine when possible.
 8. Substantial meals.
- b. Nonspecific Measures:
 1. Indirect transfusions, small, and repeated if hemoglobin 65 per cent or under and R.B.C. 3,000,000 or less.
 2. A few cases were treated with an intrauterine injection of carbolic in glycerin (1-16).
- c. Special Measures: Intravenous and intramuscular into each buttock, injections of scarlet fever antitoxin (30 to 45 c.c.). This was repeated once within thirty-six hours and in three cases twice within thirty-six hours.

Group II:

(101° to 102° F. for twenty-four hours.)

- a. General Measures, as outlined.
- b. Nonspecific Measures: when necessary.
- c. Special Measures: 30 to 45 c.c. of scarlet fever serum intramuscular into each buttock.

Group III:

- a. 100° to 101° F. for twenty-four hours: These cases were isolated, watched carefully and given ergot and quinine, and plenty of fluids.

b. No elevation of temperature:

These cases were placed in the same end of the ward and watched.

If the temperature of any of the cases in Groups II and III should rise, they would be treated according to the measures of the groups into which they would fall.

TABLE III. PUERPERAL SEPSIS DUE TO STREPTOCOCCUS HEMOLYTICUS, 1927-28. RECORD OF CASES. BURNSIDE, TORONTO GENERAL HOSPITAL

GROUPS	TREATMENT	RESULTS
Group I 102° F. or over for twenty-four hr.	1. General measures 2. Nonspecific when necessary 3. Scarlet fever serum (intravenous and intramuscular)	Positive cultures 4 Deaths 1 Total 17 cases
Group II 101-102° F. for twenty-four hr.	1. General measures 2. Nonspecific when necessary 3. Scarlet fever serum intramuscularly	Total 6 cases
Group III (a) 100-101° F. for 24 hr. (b) No temperature	(a) General measures (b) Watched	(a) 9 (b) 20 Total 29

Results.—Seventeen patients during this period of two years (1927-28) were considered to be seriously ill and included under Group I. Six of these cases were transfused one or more times and the 17 cases received scarlet fever serum intravenously and intramuscularly. Of the 17 patients, 4 were found to have positive blood cultures showing *Streptococcus hemolyticus*. There were 3 recoveries from these and one death. This is the only fatality in the public obstetric wards caused by *Streptococcus hemolyticus*, from the Spring of 1926 up to the present date. In this fatal case, we found the *Streptococcus anhemolyticus* in the genital tract, but not the *Streptococcus hemolyticus*. Later on the latter was found in the urine and blood culture. We gave scarlet fever serum intramuscularly, because with the report of the *Streptococcus anhemolyticus*, it was not a typical case of puerperal sepsis. It is quite possible that this infection did not arise in the genital tract, but I feel now that an intravenous injection of scarlet fever serum might have helped.

In Group II there were 6 cases, all of whom received scarlet fever serum intramuscularly. In the third group, there were 9 cases showing a temperature from 100° to 101° F. and 20 cases with positive cervical swabs and no temperature.

SUMMARY

Septic Abortions.—The cases which recovered were treated within three days of onset of infection.

Puerperal Sepsis.—All *Streptococcus hemolyticus* patients died. They were not treated until one to three weeks after the infection.

TABLE IV. RESULTS GYNECOLOGIC WARDS (JUNE) 1926-27-28, SEPTICEMIAS FOLLOWING

A. Septic Abortions

ORGANISM		TREATMENT	RESULTS	
a. Streptococcus hemo-lyticus	8	(a) and (c) cases	<i>Deaths:</i>	
b. Staphylococcus aureus	1	1. General measures	Streptococcus hemo-ticus	3
c. Unproved	2	2. Nonspecific	Staphylococcus aureus	1
		3. Scarlet fever anti-toxin intravenously and intramuscularly	Unproved	2
			<i>Recoveries:</i>	
			Streptococcus hemo-lyticus	5
Total 11			Total	11

B. Puerperal Sepsis

ORGANISM		TREATMENT	RESULTS	
a. Streptococcus hemo-lyticus	4	a. Cases	<i>Deaths:</i>	
b. B. coli	1	1. General measures	Streptococcus hemo-lyticus	4
		2. Nonspecific measures	<i>Recoveries:</i>	
		3. Specific measures	B. coli	1
		b. Mercurochrome intrave-nously		
Total	5		Total	5

The essential point of the whole question of treatment in puerperal sepsis is that the measures used should be begun as early as possible. In order to do this, we must have a systematic plan of investigation in every case of temperature in the puerperium. This plan of investigation should include a culture of the cervical discharge and this procedure should never be neglected. Besides the general and nonspecific measures of treatment which are fairly well known, we have used since 1926, scarlet fever antitoxin as the special measure in the treatment of puerperal sepsis due to Streptococcus hemolyticus. This serum was chosen because its immunizing power against one of the family of hemolytic streptococci could be measured. A specific type of hemolytic streptococci has never been proved to be the cause of puerperal sepsis. If this is true, it would be impossible to produce a specific serum against puerperal sepsis. The value of the scarlet fever serum may be due to:

1. A nonspecific unmeasurable power which is shown by a beneficial clinic result.
2. A production of immune antitoxic bodies.
3. A stimulation of the various defensive powers of the blood stream, such as the opsonic and phagocytic power of the white corpuseles and the bactericidal power of the serum.

It would appear that the stimulation of this defensive mechanism is the most natural method of combating in a special way an infection of this nature. The results obtained in these cases reported are very encouraging and they would seem to clearly justify its further use. However, one must distinctly remember that the outlook depends upon early diagnosis and early treatment.

CONCLUSIONS

1. Thirty-two per cent of morbidity in the cases reported were due to puerperal sepsis and in over 50 per cent of these, the *Streptococcus hemolyticus* was the causative organism.
2. The *Streptococcus hemolyticus* was found to be:
 - a. Seasonal in appearance.
 - b. Occasionally present in the genital tract during pregnancy, more often during labor, and most often in the puerperium.
3. The *Streptococcus hemolyticus* when found in the cervical canal during the puerperium is always a source of danger.
4. Early investigation and immediate treatment of puerperal sepsis cases is essential.
5. Scarlet fever antitoxin has a special value in the treatment of puerperal and postabortal cases of sepsis due to the *Streptococcus hemolyticus*.
6. Finally, further investigation on this subject is necessary. The possible value of antenatal immunization for all patients would seem to offer a fruitful research problem.

I wish to thank Dr. Donald Fraser of the School of Hygiene for his kindly interest, together with his invaluable help in this work. I am also grateful to Dr. Gordon Cameron for his careful bacteriologic examinations and reports.

Green, Armytage, V. B.: A Case of Torsion of a Fallopian Tube and Ovary During Pregnancy. J. Obst. & Gynec. Brit. Emp. 36: 87, 1929.

A sixteen-year-old girl, five months pregnant, presenting severe abdominal symptoms was laparotomized. The findings were: serous fluid in the abdominal cavity, adherent omentum, right tube and ovary twisted $2\frac{1}{2}$ times in the longitudinal axis close to the fundus, with partial gangrene. The tube and ovary were removed. The latter contained a corpus luteum. The patient delivered normally several months later. Complicating the convalescence following operation were kala azar, and the presence of various intestinal parasites.

FRANK SPIELMAN.

HYPERTHYROIDISM ASSOCIATED WITH PREGNANCY*

By J. WILLIAM HINTON, M.D., F.A.C.S., NEW YORK CITY

(Assistant Professor of Surgery, New York Post-Graduate Medical School and Hospital. Assistant Attending Surgeon Bellevue Hospital. Assistant Attending Surgeon, St. Mark's Hospital)

IT IS a well-known fact that pregnancy is frequently accompanied by a hypertrophy of the thyroid gland. According to the more conservative the number of women thus affected is 40 per cent, while others place it as high as 90 per cent. These percentages vary according to whether they are taken from a goiter belt or from a seacoast community. Some refer to this condition as a physiologic enlargement of the thyroid but whether it be physiologic or pathologic is not settled, though the evidence at present would indicate it to represent a diseased thyroid state. We are referring to a primary enlargement during pregnancy and not a preexisting goiter which is aggravated by pregnancy. That excessive demands are made upon the thyroid at this time is borne out by multiparae showing evidence of thyroid enlargement during the fifth month, while primiparae do not show evidence of it until the sixth month. There are three types or stages of goiter, which include colloid, adenomatous, and exophthalmic goiter or Graves's disease. Whether these conditions represent separate diseases or stages of the continuous process is still unsettled, but Hertzler³ has led us to believe that the different types of goiter merely represent stages in a continuous process. His work is also borne out by Rienhoff⁵ and Hellwig.² In studying histologic sections of the thyroid in stillborn infants and in persons to eighty-nine years of age who met with accidental death, we have been forced to conclude that a correct diagnosis of thyroid diseases cannot be made from either the clinical picture or the histologic sections alone, but these must be studied together before arriving at a final diagnosis.

There are two types or stages of hyperthyroidism: (1) Adenomatous or nodular goiter. (2) Exophthalmic goiter or Graves's disease. It is essential to understand the fundamental differences in these two types or stages of hypersecretion. Some clinics go so far as to make definite clinical entities out of the above conditions, stating that they are separate diseases and not interchangeable, and that the management for one condition is different from the other, but at the present time this distinction does not seem warranted. Plummer⁴ has maintained that the hyperthyroidism of exophthalmic goiter was of a different type than the hyperthyroidism of adenomatous goiter and that iodine or Lugol's solution would be beneficial in the former but contraindicated

*From the Goiter Clinic of St. Mark's Hospital.

in the latter as a preoperative medication. Graham¹ proved that iodine was beneficial in both types preoperatively, but the quantity necessary to improve the adenomatous goiter was less than that for an exophthalmic goiter. It is very difficult to make a clinical classification which coincides with the histologic sections and one is not infrequently surprised when he has made a clinical diagnosis of adenomatous goiter with hyperthyroidism to receive a pathologic diagnosis of Graves's disease. The same holds true in typical cases of exophthalmic goiter that have received iodine therapy.

The following cases will illustrate the difficulties encountered if one relies on the history and physical findings on the one hand, or the histologic sections on the other.

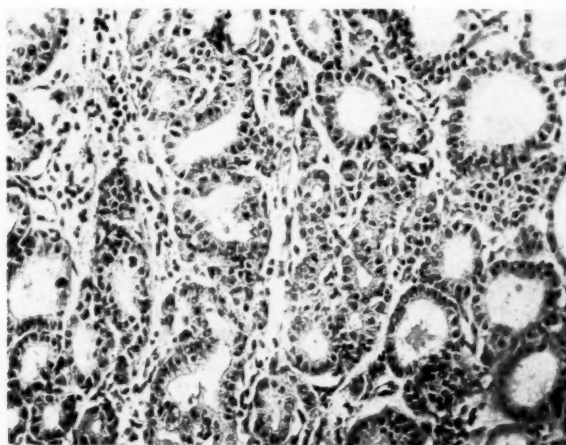


Fig. 1.—Diffuse epithelial hyperplasia with high columnar epithelium, narrow lumen with infolding and with little colloid. Active stage.

CASE 1.—Female, thirty-eight years of age, a nurse, was first seen by me on August 4, 1927; she stated that twelve years previously she had been operated upon for an adenoma of the isthmus of the thyroid. About one year after this operation she noticed a lump in the right side of her neck. This had increased slightly in size and about seven weeks before consulting me she had a gastrointestinal upset from eating sea food. Since that time she had lost 20 pounds in weight, and has had palpitation of her heart, and shortness of breath on going upstairs. Otherwise she felt well. Her menstrual periods had been scanty during the last few months. Examination: There was no evidence of exophthalmos in the right eye. The left eye had been enucleated following an accident at the age of two years. At the time of examination there was a nodular mass involving the right lobe without a thrill and her pulse was 108. A diagnosis of adenoma of the thyroid with hyperthyroidism was made. Basal metabolism on August 4 was a plus 45. The patient was advised to enter the hospital for operation, which she did, and was operated upon on August 22, 1927. She made an uneventful recovery, being discharged from the hospital on August 30, 1927. Pathologic report: Hyperplastic goiter of Graves's type, in a stage of remission at the time. See Fig. 1. This case was considered a typical adenomatous goiter with hyperthyroidism and an exophthalmic goiter was not suspected until receiving the pathologic report.

CASE 2.—Female, twenty-six years of age, was first seen by me on November 30, 1927 complaining of a swelling in her neck which she had had for one year. Friends first noticed a lump in the right side of her neck but at that time she had no symptoms referable to her goiter. Occasionally a sensation of pressure and choking were noticed but otherwise she felt perfectly well. Examination was negative, with the exception of a definite mass involving the right lobe of the thyroid. The left lobe was negative. Weight $133\frac{3}{4}$ pounds, pulse 100. Diagnosis of adenoma of the thyroid was made and basal metabolism on December 2, 1927 was plus 3. Patient was informed she had the type of goiter that could not be treated by medication, but as I had treated her sister for a colloid goiter with a satisfactory result, she demanded medication before submitting to an operation; hence she was put on thyroid extract, 1 grain t. i. d. The patient was next seen on January 18, 1928 at which time her weight was $137\frac{1}{4}$ pounds and pulse 90. She had no complaints but her neck remained unchanged and she was given thyroid extract, $\frac{1}{2}$ grain t. i. d. On March 21, 1928 she returned stating she had nausea and vomiting and had been bothered with diarrhea for two weeks and was begin-

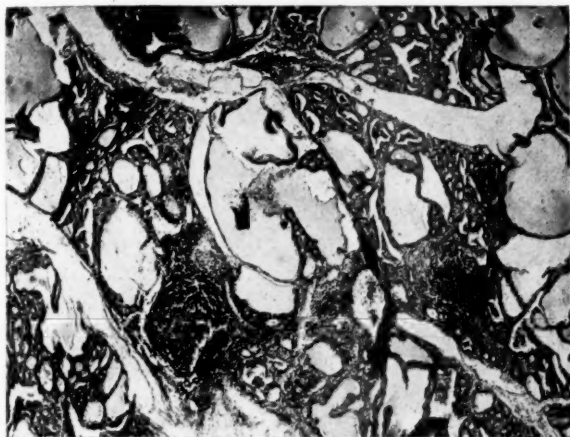


Fig. 2.—Diffuse epithelial hyperplasia. Some areas show narrow alveoli with little colloid and high epithelial lining, others contain much colloid. Numerous lymph follicles in stroma.

ning to feel ill. She complained of nervousness and palpitation and was losing weight. Examination revealed an enlargement over the thyroid region with a definite thrill over it, and a beginning exophthalmos. Diagnosis then made of exophthalmic goiter. Patient was advised to enter the hospital for observation and operation, which she did on March 22, 1928. Basal metabolism on March 26, 1928 was a plus 60. Weight was 105 pounds and pulse 160. The patient was operated upon on April 2, 1928 and made an uneventful recovery. Pathologic report: Exophthalmic goiter in the stage of remission Fig. 2. From the course of this case one can see a nodular type of goiter changed clinically to an exophthalmic goiter by thyroid medication.

CASE 3.—Female, thirty-three years of age, stated that in September, 1927 she consulted her family physician for a swelling of her left ankle and a goiter. At that time she was found to have a phlebitis of the left ankle. On communicating with Dr. Felder, her family physician, I found the patient had a colloid enlargement of her thyroid, without symptoms. The patient was not given any thyroid or iodine medication but five months later, as her mother had died from an

exophthalmic goiter, she consulted a thyroid specialist in New York, for she was rather conscious of the slight fullness in her neck. There were no symptoms referable to the thyroid at that time. Basal metabolism February 4, 1928 was a minus 1. She was informed that she had no thyroid disturbance but was given Lugol's solution 3 minims, t. i. d. Three months later she had lost 8 to 10 pounds in weight, her eyes were enlarged and she was nervous and quite irritable, and bothered with palpitation. She consulted another physician who told her she had

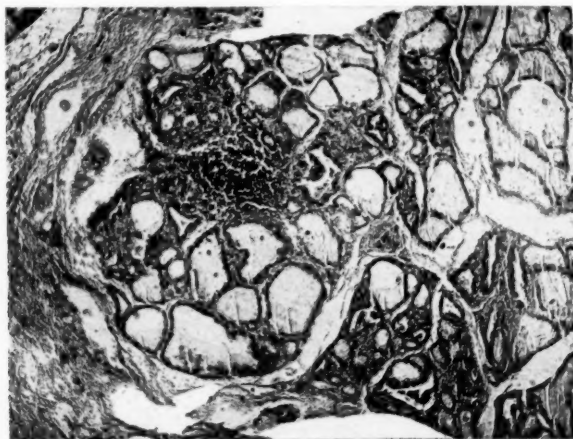


Fig. 3.—Diffuse epithelial hyperplasia with infolding, in some areas more marked than in others. Lymph follicles in stroma. Relatively low activity is shown best by increase of colloid secretion.

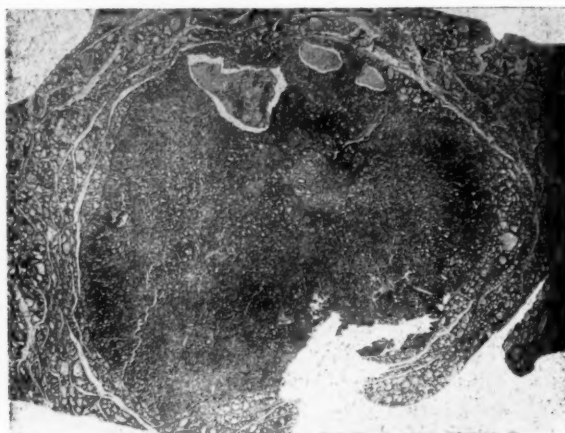


Fig. 4.—Very low magnification shows circumscribed adenoma.

Graves's disease. The patient was given 1 grain of iodide of mercury daily, and advised to have roentgen-ray therapy. She received several treatments and showed improvement but four months later, not feeling entirely well, she consulted Dr. Carter at which time her weight was 118 pounds, as against her best weight of 135 pounds. Basal metabolism on October 27, 1928 was 3 below the average normal. I saw this patient in consultation with Dr. Carter on October 28, 1928 at which time there was definite evidence of enlargement of the thyroid with a thrill over it, and it was quite apparent that the patient was suffering from an

exophthalmic goiter. Thyroidectomy was performed on November 5, 1928 by Dr. Carter. Pathologic diagnosis: Exophthalmic goiter in resting stage. (See Fig. 3.) One sees a colloid goiter which was changed into an exophthalmic goiter by iodine administration.

CASE 4.—Female, forty-five years of age, first seen June 2, 1927 complaining of nervousness, tremor of fingers, swelling of neck and protruding eyes, from which she had suffered for a period of five years. Her symptoms came on following the



Fig. 5.—Capsule of adenoma with adenoma on one side, and diffuse epithelial hyperplasia on the other.

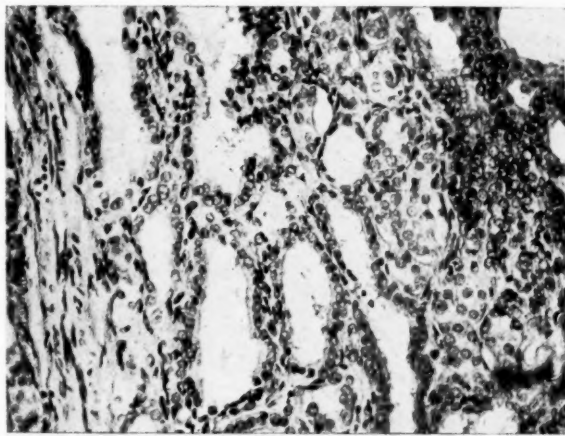


Fig. 6.—High-power magnification showing diffuse epithelial hyperplasia. Little colloid. Epithelial lining is high.

death of her daughter from pneumonia. The patient had had a cholecystectomy and appendectomy ten years previous to the time she consulted me; otherwise her history was negative. Examination revealed bilateral exophthalmos with symmetrical swelling of thyroid and thrill over it. The heart was fibrillating and the pulse could not be counted accurately. Basal metabolism on May 28, 1927 was a plus 69. Weight 157 pounds with pulse 150. The diagnosis of exophthalmic goiter was made and the patient was operated upon on June 11, 1927. Pathologic report:

Exophthalmic goiter in a resting stage, with two small adenomas. (See Figs. 4, 5, 6.) In this case the histologic sections revealed an adenomatous goiter and exophthalmic goiter in the same person which does not lead one to believe that they are separate clinical entities.

In view of the fact that the histologic findings in the above cases did not coincide with the clinical picture, we have taken sections from people whose deaths were due to accidental causes to determine whether the histologic findings are constant for different ages in life.

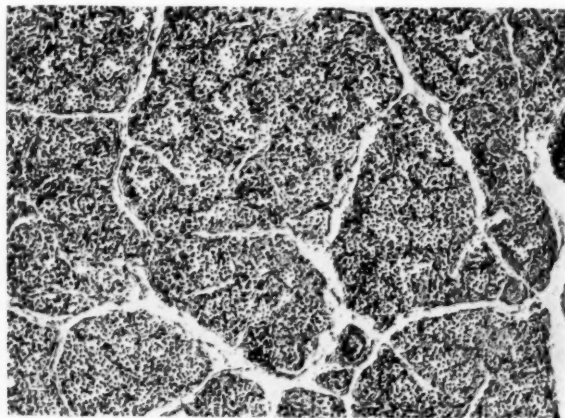


Fig. 7.

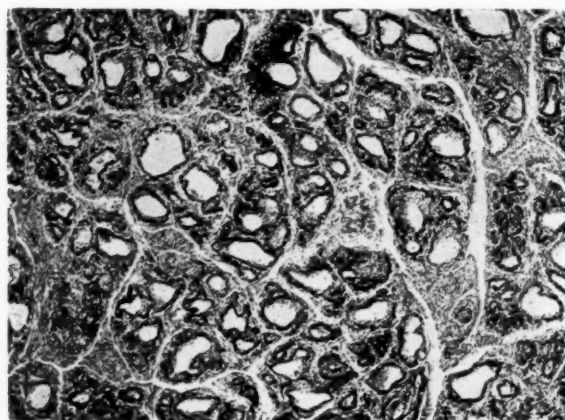


Fig. 8.

Fig. 7 is a section from a stillborn female baby, with cranial injuries. The section reveals epithelial cells divided into lobules by connective tissue and no definite formed acini. This represents what is usually found in fetal thyroids. Fig. 8, male, ten weeks of age, died from a rupture of the spleen. In this section one notes the acini well formed containing colloid with a marked amount of interacinal connective tissue. This section is so well developed that one might mistake it for an adult thyroid. Fig. 9, male, aged thirteen, cause of death

fractured skull. The section reveals very large acini containing colloid in parts of the section, while in other fields there are numerous epithelial cells closely spaced. Fig. 10, female, aged thirty-five, cause of death fractured skull. This section reveals one or two developing acini while most of the section contains dense masses of epithelial cells with connective tissue dividing the gland into lobules. The histologic picture in this section is more of a fetal type. Fig. 11, male, aged twenty-five, shot and instantly killed. This section reveals the acini large and dilated containing dense colloid material, showing a marked contrast with Fig. 10.

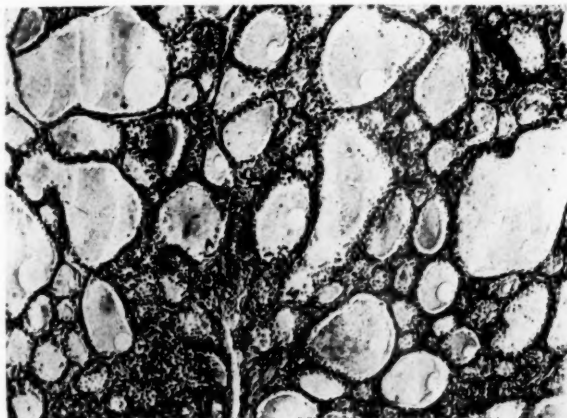


Fig. 9.

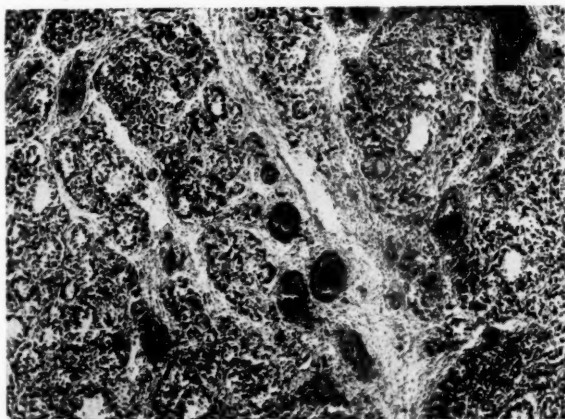


Fig. 10.

Fig. 12, female, aged sixty-one, committed suicide by strangulation. The section reveals epithelial cells closely spaced with some very small acini. The general appearance of this section is similar to that of an infant thyroid. Fig. 13, male, aged seventy-five, fractured skull and lacerated brain. This section reveals some well-developed acini containing colloid but in other parts the section reveals epithelial cells that are closely spaced with fibrous tissue forming a definite lobule. This section is more characteristic of an infant's thyroid than that of a man seventy-five years of age.

From the above sections it can be seen there is a marked variation in the histologic picture of the thyroid of people in apparently normal health who met with accidental death.

It is essential to look upon hyperthyroidism during pregnancy as one continuous process and not as separate diseases. From the above cases it can be seen how difficult it is to be certain of a diagnosis unless the

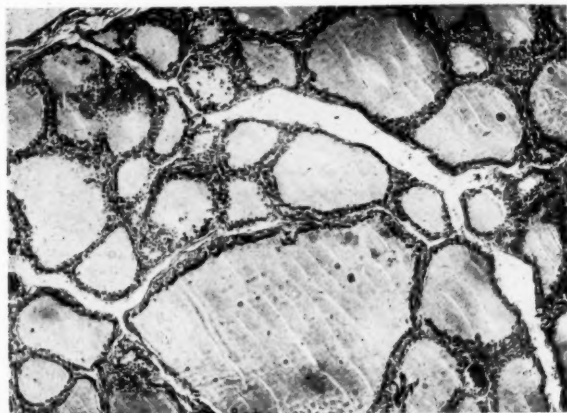


Fig. 11.

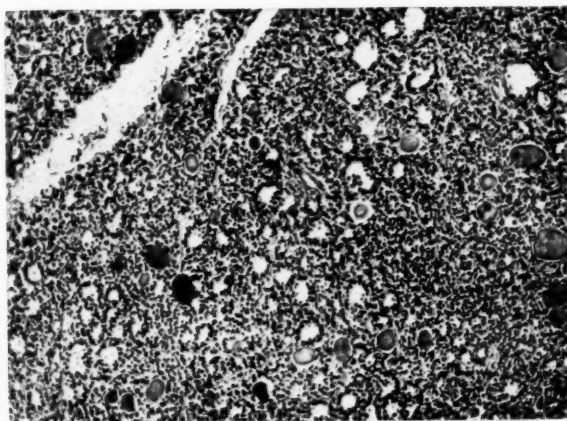


Fig. 12.

clinical findings and histologic sections are studied together, but for the clinical management of the patient it is essential to divide them into acute and chronic stages of hyperthyroidism, or exophthalmic goiter and adenomatous goiter.

Treatment.—Chronic hyperthyroidism, or hyperthyroidism from a nodular or adenomatous goiter usually occurs in women who have borne several children in rapid succession and who say an enlargement of

the thyroid was noticed after the birth of the first or second child, while the symptoms of hyperthyroidism may not develop until after the third or fourth pregnancy. What should be done in this type depends to a great extent upon the patient's condition and her desire to have more children. If the case is clinically mild with a metabolic rate not exceeding a plus 30, the patient can, in all probability, be carried through a normal pregnancy without any undue risk of permanent cardiac damage. But if the patient at the beginning of pregnancy has a high metabolic rate with a definite cardiac involvement, termination of pregnancy is advisable, and if the patient does not wish to submit to that the only alternative is a thyroidectomy after proper preoperative treatment.

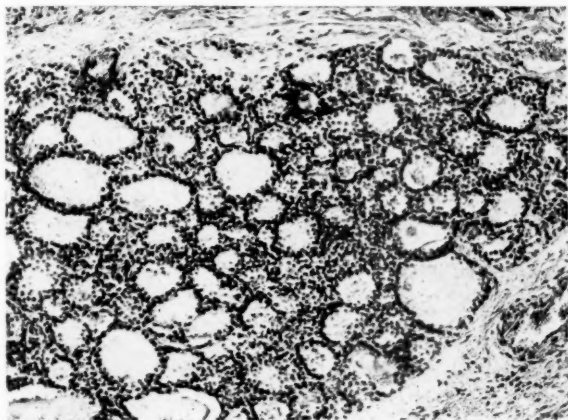


Fig. 13.

Exophthalmic goiter or Graves's disease usually develops in the early months of pregnancy, and more frequently in primiparae. The management will depend entirely upon the condition of the patient when first seen. Unless she is critically ill it is not necessary to interrupt the pregnancy but a thyroidectomy can be performed and the patient carried through a normal delivery. If the case is very mild it may be possible to carry the patient through her pregnancy on medical management and defer more radical measures until later.

Comment.—The two types of cases which need pregnancy interrupted are: First, chronic hyperthyroidism associated with the nodular or adenomatous goiter in which there is a definite myocardial degeneration; and second, cases of exophthalmic goiter or Graves's disease which are of a fulminating type and which endanger the life of the mother by allowing the pregnancy to continue. It is safe to estimate that 90 per cent of cases of hyperthyroidism associated with pregnancy can be carried to a normal delivery if properly managed.

REFERENCES

- (1) *Graham, A.*: J. A. M. A. 87: 628-631, 1926. (2) *Hellwig, C. A.*: Surg., Gynec. Obst. 47: 173-179, 1928. (3) *Hertzler, A. E.*: Arch. Surg. 16: 61-78, 1928. (4) *Plummer, H. S., and Boothby, W. M.*: J. Iowa State Med. Soc. 14: 66-73, 1924. (5) *Rienhoff, W. F.*: Arch. Surg. 13: 391-425, 1926.

125 EAST SEVENTY-SECOND STREET.

PREGNANCY CONCOMITANT WITH ASTHMA OR HAY FEVER

By A. C. WILLIAMSON, M.A., F.A.C.S., PITTSBURGH, PA.

THERE is no patient more distressing or uncomfortable to herself and others than the asthmatic or hay fever victim. The asthmatic is distinctly a law unto herself, and in each instance a painstaking and meticulous history is necessary if relief is at all possible and if discovery of the cause is imminent. It would appear probable that pregnant patients would suffer more annoyance and that the dangers of miscarriage would be more possible than ordinarily. The questions arising are: Is miscarriage more frequent in asthmatics and hay fever patients than in others? Does the time of pregnancy, the trimester, have an effect, or is it influenced by the preexisting condition? Can the patient be treated during a pregnancy, i.e., the desensitizing of a known pollen type, without danger to the pregnancy? Is there any special influence on the infant or not? The following case presentations with their histories are interesting and curious and assuredly bear out the statement that the asthmatic or hay fever patient is distinctly a law unto herself.

GROUP I. ASTHMA

CASE 1.—Mrs. C., white, age twenty-eight years, para ii. Normal in every way except for asthma which began with onset of her periods at the age of thirteen years. For eleven years she has averaged two attacks monthly, but there seems to be no definite periodicity from a standpoint of etiology. The attacks are "terrific," lasting from four hours up to three days and followed by "collapse," necessitating one to three days in bed. She has tried all the usual remedies with little or no relief and now requires large doses of morphia during attacks. During her first pregnancy she had no attacks until just before delivery; the attack then was not severe. Her labor lasted seventeen hours. She was delivered under gas-oxygen; an easy low forceps delivery. She nursed her baby for seven months and had no attacks until weaning—when the old twice-a-month régime again was inaugurated. With the second pregnancy she had two mild attacks at the third and seventh months. Her labor was short, delivery spontaneous under gas-oxygen. During both pregnancies she was troubled with a skin irritation which could only be relieved by a liquid diet and the use of paraldehyde as a soporific.

CASE 2.—Mrs. R., white, age twenty-seven years, para i. She has had severe attacks since she was four years old, whenever she has been tired or "nervously upset." Her pregnancy was comparatively comfortable until the seventh month, from then on attacks at approximately twelve-day intervals. Her labor was of twenty-four hours' duration; just before full dilatation an asthmatic attack lasting for three hours occurred. Morphia and adrenalin did not help. At full dilatation,

gas-oxygen was attempted, a 40 to 60 mixture, but was useless until 25 per cent ether was added, then the patient began to breathe easily in about six minutes. Delivery was an easy low forceps, but patient went into moderate shock, pulse at the wrist not being picked up for two hours. Digitalis was started with the idea of supporting the heart. Fourteen hours after delivery another severe attack, with the pulse climbing to 168 and temperature 101°. Morphia and adrenalin were of no avail, a few breaths of ether gave immediate relief, the patient dropped off to sleep, woke three hours later, again the attack began and relief was impossible, the pulse climbed steadily, heart dilated, and seven hours later she died. Autopsy revealed emphysema in lungs, a particularly thinned-out, flabby heart muscle with definite myocardial changes. The baby was apparently normal.

CASE 3.—Mrs. H., white, age thirty-six years, para iv. The patient has been "asthmatic" since sixteen years of age, having about eight attacks yearly with no definite periodicity or etiology. She has had two boys and two girls. During gestation with the girls she was free from attacks and after delivery nursed the girls up until the sixth month, and during lactation there were no attacks. During the pregnancy involving the two boys, she was troubled with marked nausea and vomiting and had four and three terrific attacks of urticaria respectively. Both boys were sensitive to egg albumen, and one child at five years is an "asthmatic" apparently, and the other boy at seven apparently is suffering from rose fever, although skin tests show several food and plant idiosyncrasies as well. The labors were all easy and spontaneous.

CASE 4.—Mrs. H., white, age twenty-five years, para i. Asthmatic attacks began at the age of fifteen years, simultaneously with first period, and since then they have occurred at any time. She thinks they usually come when she is particularly tired or constipated. Skin test showed reactions to several foods, to a few pollens and to horse hair, but in her manner of life the exact etiology of these must be doubted. She has always been subject to "colds" and is never free from "catarrh." Her one pregnancy was a comfortable one, and she had no attacks during the period of gestation or lactation. Seven weeks after weaning her baby she again had an attack but not quite so severe and in the last two years the attacks have been as frequent but not so severe as formerly. Her baby has no idiosyncrasies of any sort as far as protein sensitization is concerned.

CASE 5.—Mrs. K., white, age thirty-two years, para ii. She has been an asthmatic since the onset of menstruation at sixteen. She averages four severe attacks and possibly six minor attacks during the year. During her first pregnancy, resulting in a boy, she was without attack and had none until she weaned the child at eight and a half months. During her second pregnancy, with a female, she was nauseated and decidedly uncomfortable from urticarial attacks and skin irritations. She had one severe seizure at the third month, and at postpartum had attacks apparently as before despite nursing the child. The infant had severe eczema and was markedly sensitive to cow's milk and egg albumen.

CASE 6.—Mrs. M., white, age thirty years, para iii. Her first attack occurred eleven years ago, a month after coming to America. Since then she has had to guard against fatigue and overeating. She says the attacks were less severe during her pregnancy, and yet five hours after her third delivery she developed an acute attack lasting sixteen hours, scarcely relieved by adrenalin or morphia. During lactation she was relatively free from attacks. Her baby had marked eczema from the third to twenty-first months but had no one special food idiosyncrasy.

CASE 7.—Mrs. K., white, age thirty-six years, para iii. She has been an asthmatic since she was sixteen years old and thinks the attacks began with the onset of menstruation. There has been no special periodicity of attacks, but there has always been an attack when she has been particularly tired. Her general health has been good except for a "catarrhal condition" and susceptibility to "colds."

She has been free from attacks during each gestation except that while she was pregnant with the second child—a boy—an annoying urticaria caused much annoyance. She was unable to nurse the two boys and her asthmatic attacks began almost immediately. She nursed the girl and had only one attack during lactation and that was at the fifth month.

CASE 8.—Mrs. H., white, age thirty-two years, para i. Has been an asthmatic as long as she can remember. She has been usually well, aside from frequent colds. During pregnancy she had no attacks, the labor was short and easy. During lactation she had no attacks, and it was the first time she had always been free from her difficulty.

CASE 9.—Mrs. K. C., white, age thirty-two years, para ii. Her asthma began at the age of fourteen years, a year after the onset of catamenia. The attacks always seemed to follow a period of being tired or quite "upset nervously." During both pregnancies the nausea was persistent and at intervals would terminate in an asthmatic attack lasting for twenty-four to thirty-six hours, unrelieved by the usual remedies. During lactation there was no change. Her baby had eczema up to the eighteenth month.

CASE 10.—Mrs. C., white, age forty-one years, para iv. She has been an asthmatic since a "small child." There is no time interval between attacks, but their frequency has increased in the last four years with practically no relief from the use of adrenalin or morphia. With the third pregnancy she was in bed from the eighth month onward, and with the fourth she was in bed from the sixth month because of a failing heart. She was unable to nurse her children. The first child had severe eczema until twenty-two months old and now at eleven years is a confirmed asthmatic.

CASE 11.—Mrs. D. A., white, aged twenty-six years, para iii. She came to this country from Italy and had her first attack at seventeen, her first autumn here; since then her attacks have occurred almost once a month, at her menstrual period without fail. Her pregnancy and lactation periods seem to have no bearing on the condition. This pregnancy and labor were uneventful, but on the fifth day post-partum a severe attack lasting ten hours occurred, relieved only by large doses of morphia. Her children are apparently well, with no complicating idiosyncracies as far as skin or food are concerned.

CASE 12.—Mrs. D. S., white, age twenty-five years, para i. The onset of attacks dates back nine years. The attacks are at any time during the year and practically have made an invalid of her for four years. Following an attack of tonsillitis, three years ago, a diagnosis of severe mitral stenosis was made. Cesarean section with sterilization under local anesthesia was refused. The labor lasted twenty-one hours and was terminated by an easy low forceps delivery with nitrous oxide-oxygen anesthesia. Her pulse rose to 168, temperature to 101.6°. For forty-eight hours she was on the verge of decompensation but quieted gradually through the generous use of morphia and digitalis. After twenty days' rest in bed, her pulse dropped to 96 and her convalescence was uneventful, she became restless and insisted on going home against advice. She was warned of the dangers but in spite of this attempted to get out of bed four days later, precipitated an asthmatic attack and died four hours after the onset.

CASE 13.—Mrs. D., white, age twenty-three years, para i. Her first attack of asthma was at the age of fifteen years; since then she has had about eight severe attacks a year. If "she does not get tired or catch cold," she has no attacks. During her pregnancy the hyperemesis was severe. At the seventh month she developed eclampsia and spontaneously delivered a stillborn infant. She recovered promptly. An asthmatic attack occurred on the ninth day but was immediately relieved by adrenalin.

GROUP II. POLLEN TYPE

CASE 1.—Mrs. H. E. S., white, age thirty-one years, para iv. She is troubled with the "goldenrod" variety. When a child, she had a mild reaction to eggs. For eleven years she has been increasingly annoyed with the condition. She had a miscarriage at two and one-half months. Her two successful pregnancies ended in November and February. She was given vaccine during her fourth pregnancy, the initial dose beginning two months previous to pregnancy. She obtained no relief, but the season during her pregnancies was relatively mild.

CASE 2.—Mrs. M., white, age twenty-six years, para i, has had "rose fever" for eleven years. She had two years of vaccine treatment starting during the second month of pregnancy with no ill effect. The relief by reason of vaccine has been remarkable. The attacks were so annoying that it was considered necessary to initiate treatment. During gestation urticaria was frequent and annoying, but she did not obtain relief by alkalization. The labor was uneventful as was the postpartum convalescence.

CASE 3.—Mrs. H., white, age thirty-seven years, para v. She has had hay fever since seven years of age, August and September being the particularly troublesome months. Goldenrod seems to be the offending agency. She received treatment during the second and third pregnancies—on one occasion during the first trimester and the second time during the second trimester with no ill resulting. The relief was so slight that she refused to bother with more immunization. With male pregnancies she suffered from severe urticaria, but no discomfort when pregnant with female. Both boys had marked eczemas—one is a severe asthmatic, the other has apparently nothing more than the childhood eczema. Fortunately all labors were short and uncomplicated.

CASE 4.—Mrs. R., white, age twenty-six years, para ii. This patient suffers also from goldenrod variety, the attacks began, she thinks, with the onset of catamenia at the age of fourteen years. During her first pregnancy immunization was attempted at the middle of the first trimester and she miscarried at third period. She went through a second pregnancy with little difficulty except for a severe urticaria which seemed to occur with some relation to the time of period. The baby had a moderately severe eczema until the twentieth month and showed a marked reaction to eggs.

CASE 5.—Mrs. G., white, age thirty-one years, para iii. She has been troubled for twelve years, the attacks beginning about the middle of May and continuing until July. She has been pregnant twice during this time and had no apparent difficulty. Of the children, the boy had eczema badly, the two girls had no trouble at all. She does not think that pregnancy influenced her attacks in any way.

CASE 6.—Mrs. B., white, age twenty-seven years, para i. The paroxysms of sneezing begin the middle of August and continue through September. They began apparently with the onset of catamenia, fourteen years before. She had the attacks during the sixth and seventh months of gestation with practically no variation in severity. Labor was short and easy, normal in every way. The baby also was apparently normal but died suddenly on the third day and the death was termed a thymic one.

CASE 7.—Mrs. O'C., white, age twenty-three years, para i. She has always been a healthy person aside from an annoying idiosyncrasy of nasal irritations and frequent cold. For five years she has been subject to what was termed rose fever, and despite the pregnancy the affair was so serious she determined to begin a course of treatment. The inoculations were carried out from the fourth to sixth month of pregnancy with no apparent ill effect. Labor was easy and the baby well; there

were no skin eruptions, but the patient was unable to take anything with egg used in any way.

CASE 8.—Mrs. L., white, age thirty-nine years, para ii. Fibroid uterus. She has hay fever attacks beginning in early July and continuing throughout to mid-September. She dates their beginning when about fifteen years old. Skin testing has shown a variety of causes, hence she refused inoculations as an attempted remedy. Her second pregnancy at the fourth month on carried through the period, and she thought that she was not as distressed as usual. Labor was uneventful, but the baby had an eczema lasting for twenty months and now at four years old is apparently developing into a typical asthmatic.

CASE 9.—Mrs. S., white, age twenty-six years, para i. The condition has been present for nine years, and she thinks it gets a little more severe each year. For three years she was treated, and although the cause seems to be definitely goldenrod, she has no relief. Her labor was normal, and everything was well until the fifth day, when she developed a frightful urticaria which would not respond to treatment. Bromides and opiates were all employed; ephedrine and adrenaline were of no avail, and after three sleepless days and nights the condition disappeared almost at once. The baby apparently is well and free from skin troubles.

CASE 10.—Mrs. K., white, age twenty-six years, para i. The etiology here is definitely in the rose fever class. Inoculations were carried out during the second and fourth months of pregnancy with no ill effects but with a definite lessening of the severity of the attack during the year. The pregnancy was uneventful, but the baby has a nasty eczema which will appear at regular intervals for no reason at all.

CASE 11.—Mrs. C., white, age twenty-seven years, para iii. This patient was born in the South and had no trouble until her first visit North seven years ago. During the entire residence in the North the trouble has begun late in May, lasting well up until the middle of July. The boy had eczema badly, and during this gestation she was free from attacks. Her girl had no difficulty, but she was miserable with rose fever. With the third pregnancy, also a boy, she had little trouble, and the child has been free from all attacks.

CASE 12.—Mrs. C. T., white, age twenty-two years, para ii. The first two pregnancies ended in miscarriages at the third month. An infantile uterus would offer some explanation. The fever is of the goldenrod type, and a pregnancy seemed not to affect it one way or the other. She had just as violent paroxysms of sneezing, and despite the fact that she was only in the middle third of her gestation it seemed to make no difference. The child, a girl, is seemingly free of skin difficulties.

CASE 13.—Mrs. T., white, age thirty-three years, para ii. The mother has never been a severe hay fever type. She thinks it began five years ago and that it is more severe each year. Her first child, now four years old, has been troubled with an unusually severe eczema which is persistent and unrelieved. When she was pregnant the second time, she insisted on skin testing, the cause apparently was goldenrod. The second child, also a boy, apparently has escaped the condition, and the mother is sure it was due to her being treated.

CASE 14.—Mrs. C., white, age twenty-seven years, para ii. An extremely sensitive person who dates her hay fever back nine years and attributes it to goldenrod. She has been repeatedly tested and treated with no apparent result. Her first boy had eczema mildly but had to be taken off cow's milk altogether. The second delivery occurred in July and was easy and uneventful. On the ninth day post-partum she suddenly developed an urticaria that was maddening. Nothing relieved it, and at the end of ninety-six hours it spontaneously disappeared. The second baby, a girl, has a slight eczema, but has no difficulty in handling a formula of cow's milk.

CONCLUSIONS

The study of these cases offers a variety of observations that are satisfying, and yet there is a variation of symptoms and of apparent cause and effect which is bewildering. The asthmatic group bears out almost to a patient the part played by heredity in transmitting the tendency to the disease. In no case was it known that the husband was affected, and yet practically every child showed an eczema or an idiosyncrasy toward food. It is quite generally assumed that of hypersensitive parents, both being involved, 72 per cent of children will show asthmatic signs before they are ten, and 58 per cent where only one parent is involved. We cannot substantiate this statement because the children involved are not of that age. It is a striking coincidence, however, that practically every child developed either an eczema or a food idiosyncrasy.

As far as severity of attacks go, apparently asthmatics, as such, seem to have less frequent attacks during the period of gestation and puerperium. It may be argued that it is because they get more rest and more care is taken in the prevention of constipation, together with an attempt to guard against abnormal excitement. The pollen type seems to vary not at all. A most striking observation is that the attacks with all their paroxysmal sneezings and coughings together with the unpleasant dyspnea do not seem to bring on premature labors or miscarriages. It would be fair to state that no patient had a violent attack near term, so that we could not definitely answer in regard to early rupture of membranes.

Skin testing has been rather disappointing. These patients were tried out with placenta dried, but there was no constant result which would warrant a special conclusion. It seemed to me that they were sensitive and reacted to so many reagents that it would be difficult to narrow down to an exact etiology. It is curious to note, however, that the same mother during gestation with a male child would be free from the discomfort of urticaria or "food poisonings" and yet be most sensitive if pregnant with a female child or vice versa. Equally strange is the fact, too, that one sex would have eczema and no food difficulty while the other sex would have both.

It would also seem that there is no reason why the mother should not be treated as though she were not pregnant. In the cases that have come under my observation the trimester of gestation seemed to have little to do with the treatment. The danger of miscarriage is always imminent in the first three months; if we treat a patient then and she miscarries, we are likely immediately to blame the hypodermic, when as a matter of fact there is no evidence of direct cause and effect. We would select our cases and treat them individually.

There seems to be no bearing on anesthetic, and nitrous oxide-oxygen has been completely efficacious with an occasional small percentage of ether for temporary relaxation.

FIBROMYOMA UTERI, TREATMENT AND END-RESULTS*

A REVIEW OF 254 CASES

BY F. E. KEENE, M.D., AND R. A. KIMBROUGH, JR., M.D.,
PHILADELPHIA, PA.

THIS paper represents an analytic study of 254 consecutive cases of myoma uteri admitted to the service of the senior author in the Hospital of the University of Pennsylvania from January, 1927, until July, 1929. The discussion will be limited largely to methods of treatment and end-results.

We share the commonly accepted belief that many myomas require no treatment. This applies particularly to small symptomless tumors in women who are approaching or who have passed beyond the menopause. It is our practice, however, to keep such patients under close observation, insisting upon the importance of periodic examination. Such a policy is attended by little or no risk, and many patients will be saved an unnecessary operation.

By far the greater number, however, require treatment on account of abnormally profuse bleeding, pain or pressure symptoms, and it is upon this group that our studies have been made. In this series, 62.7 per cent of the patients gave a history of menorrhagia, metrorrhagia was present in 9 per cent, lumbar or sacral backache in 27.1 per cent and pressure symptoms in 29.4 per cent.

Difference of opinion still exists regarding the treatment of these tumors. In some clinics operation is the method of choice in all cases, while others employ irradiation by either radium or roentgen rays to the exclusion of surgical measures. It is our belief that both of these plans are to be condemned; both irradiation and operation have their places in the treatment of myomas. The indications and contraindications of each are sharply defined, and the proper treatment as applied to any given case depends upon an intelligent conception of the advantages and limitations of each method.

It was the privilege of the senior author to be associated with the late Dr. John G. Clark when he first adopted radium in the treatment of benign uterine hemorrhage in 1912. During these eighteen years the patients have been carefully followed, and the rules which govern us in the selection of irradiation or operation are based upon this experience. It is gratifying to note that the indications thus formulated by Dr. Clark and his associates have been more or less generally adopted.

The following type of case we consider ideal for the use of radium;

*Read (by invitation) at a meeting of the New York Obstetrical Society, March 11, 1930.

a patient in the fifth decade of life who has a tumor not larger than a three months' pregnancy, the only symptom of which is profuse menstruation.

The contraindications to the use of radium are as follows:

1. *Tumors Larger Than a Three Months' Pregnancy.*—Such tumors often present extensive degenerative changes which are not favorably influenced by irradiation. In this series benign degenerative changes were found in 37.3 per cent, cystic degeneration was present in 21.2 per cent, calcareous in 12.2 per cent, and less frequently carneous, hyaline and liquefaction changes occurred. The larger tumors are frequently complicated by adnexal conditions, the detection of which is often impossible prior to operation. There were associated ovarian lesions in 44.4 per cent of our cases, and many of these were not suspected prior to laparotomy.

Furthermore, the blood supply of the larger tumors is very limited, and irradiation may so impair their nourishment that degenerative changes may readily occur.

Large tumors frequently distort the uterine cavity to such an extent that a thorough diagnostic curettage is precluded, and under these circumstances an area of corporeal carcinoma may easily escape detection.

While the etiologic relationship between submucous myomas and carcinoma of the fundus has never been definitely established, there is sufficient evidence to warrant removal of large tumors as a prophylactic measure. To substantiate this we cite Graves' statement that fibromyomas were associated with 25.7 per cent of his cases of carcinoma of the fundus.

2. *Rapid Increase in Size.*—Rapid enlargement of a tumor usually indicates either sarcomatous or benign degeneration, in both of which operation is demanded. Sarcoma was found in 2 of our cases, an incidence of 0.8 per cent.

3. *Pressure Symptoms.*—Frequency and urgency of urination, increasing constipation and other pressure symptoms are mechanical in origin, and their relief is dependent upon removal of the tumor. While disappearance of the tumor is a common occurrence following irradiation, the process is slow and excision is preferable.

4. *Tumors Associated With Pelvic Pain.*—Pain in association with a myoma is usually due to one of the following conditions: adnexal disease, especially chronic inflammation, degeneration of the tumor, adenomyoma, or endometrial cysts of the ovary. Radium may light up a quiescent inflammatory lesion and is to be avoided in any patient whose history suggests its presence. The frequency of this complication is evidenced by the fact that it was found in 23.3 per cent of our cases. For obvious reasons degenerating tumors should never be subjected to irradiation. Adenomyomas of the uterus often do not respond

satisfactorily to irradiation, and our experience is confirmed by Kelly who states that in the treatment of these tumors "radium is of no avail." Again, pain may be due to an associated endometrial cyst of the ovary, the treatment of which usually falls in the domain of surgery. While it may be impossible to determine prior to laparotomy the exact cause of the associated pain, the conditions revealed at operation will practically always justify the choice of surgical treatment.

5. *Pedunculated Tumors, Both Subperitoneal and Submucous Myomas*.—Radium is useless in the treatment of pedunculated tumors, and in the submucous type its action may be followed by rapid necrosis and infection.

6. *Profound Anemia*.—We hesitate to use radium in the treatment of a moderate sized tumor in the presence of severe anemia. Such patients often react poorly to it, and their diminished resistance increases the possibility of necrosis or infection of the tumor.

7. *Uncertain Diagnosis*.—The prime requisite for successful irradiation is accuracy of diagnosis. If examination under anesthesia does not reveal the exact nature of the pelvic pathology, operation is the preferable procedure.

8. *Stenosis or Blockage of the Cervical Canal*.—Irradiation of the uterine body demands that the radium be inserted well above the internal os, otherwise it may lead to partial or complete stenosis resulting in pyometra or hematometra.

9. *The Presence of Marked Secondary Anemia in Association With Tumors Not Giving Rise to Sufficient Uterine Bleeding to Account for the Anemia*.—Several such cases have come under our observation. In each, careful studies failed to demonstrate the cause of the anemia, and at operation extensive necrosis of the tumor was found. Rapid improvement of the anemia following operation warrants the conclusion that the degeneration was responsible for it.

10. *Tumors in Young Women*.—Irradiation in sufficient dosage to cause disappearance of the tumor will be followed by a premature menopause and sterility. Such patients should be treated by operation; myomectomy is the method of choice, but if this is not feasible, supravaginal hysterectomy, with conservation of one or both ovaries, is indicated.

11. *Extremely Nervous Patients*.—It is impossible to prophesy with certainty what the effect of irradiation will be in a given case so far as menopausal symptoms are concerned, but these symptoms are usually more pronounced and of longer duration in the highly nervous individual. We believe that in such patients operation with conservation of ovarian function will yield better end-results than irradiation.

12. *Radiophobia*.—We have coined this word as a contraindication because we are not infrequently consulted by patients who have an unwarranted fear of the effects of radium. If we are unsuccessful in

convincing the patient that her fear is unfounded, we choose operation even though the pelvic condition is ideally suited to irradiation. It has been our experience that when radium has been used in spite of this fear, although the pelvic lesion has been relieved, all subsequent ills may be erroneously ascribed to its lasting effects.

It is evident that with close adherence to these contraindications a large number of myomas immediately fall into the operative group. The proof of this assertion is that radium has been employed in only 21.4 per cent of our cases. Reports from our clinic show a steady decrease in the relative number of patients treated by radium. This decline in percentage does not mean that we are losing faith in the method, but rather that the contraindications are being more rigidly observed.

TABLE I. AGE BY DECADES

Third	13	5.1%
Fourth	82	32.2%
Fifth	124	48.8%
Sixth	30	11.8%
Seventh	3	1.2%
Eighth	2	0.8%
81% of patients between ages of 30-50		

TABLE II. MARITAL STATE

Single	58	22.7%
Married	196	77.3%
Parity		
Nullipara	120	47.2%
Para	134	52.8%

TABLE III. STERILITY AND FERTILITY

Incidence of sterility in married group		31.6%
One or more children	125	63.7%
Miscarriage but no children	9	4.6%
Average length of time since last child was born in parous group		16 years
Total number of pregnancies in group	450	
Number of miscarriages	105	23.3%

Radium should never be used without preliminary diagnostic curettage. Thus, valuable information is obtained as to the exact location of the tumor, as well as to the presence or absence of carcinoma of the fundus, and the possibility of an early pregnancy will be eliminated. Carcinoma of the fundus complicated 1.6 per cent of our cases. The excellent work of Murphy proves that postconception irradiation may produce disastrous effects upon the fetus, particularly microcephalic idiocy. One cannot be too careful, therefore, in ruling out pregnancy before adopting irradiation by either radium or the roentgen-ray. Irradiation for pelvic lesions should be either given by a gynecologist

who is familiar with the subject or applied under his direction. Too frequently the gynecologist is not consulted until irradiation has failed to effect satisfactory results in patients ill suited to this method of treatment.

In our analysis we find that there has been a gradual decrease in the dosage of radium. Twelve hundred milligram hours was formerly considered the standard dosage for benign lesions. This was followed by a fairly high percentage of severe menopausal symptoms which constituted the only untoward result. In this series a dosage of 600 to 900 milligram hours has diminished the incidence of severe menopausal symptoms, has satisfactorily controlled the bleeding, and has been followed by reduction in size of the tumors. Should, however, the smaller dosage be insufficient one can safely resort to ambulatory roentgen irradiation since the possibility of corporeal carcinoma has been eliminated by the curettage done at the time radium was applied.

RESULTS OF RADIUM TREATMENT

Number of cases irradiated	50
Number of cases followed up	48
General end-result excellent	83.3%
Marked improvement	10.4%
Temporarily relieved	2.1%
Unimproved	4.1%
Satisfactory results obtained	93.7%
MENOPAUSAL SYMPTOMS	
None	31.2%
Mild	39.5%
Moderate	14.6%
Severe	14.6%

Roentgen Irradiation.—A relatively small number of patients (4.7 per cent) were treated by roentgen irradiation. We believe this form of therapy is definitely indicated in certain conditions. This applies particularly to patients with large tumors, or with smaller tumors complicated by chronic adnexitis, who are poor operative risks because of a profound anemia. The bleeding can be controlled by roentgen therapy, appropriate measures can be used to combat the anemia, and if operation is subsequently necessary, it can be performed under more favorable conditions. Many patients so treated will not require operation, but there are others in whom the regression of the tumors is not satisfactory thus making their removal advisable.

Roentgen treatment may be used with comparative safety in tumors associated with chronic adnexitis, but radium often induces an acute exacerbation. Roentgen irradiation is also of value when obesity, pulmonary and thyroid complications or cardiovascular disease contraindicate operation.

As a general rule a diagnostic curettage should precede roentgen therapy, thus eliminating carcinoma and early pregnancy. Occasionally anesthesia in any form is undesirable, and in these cases diagnostic curettage may be safely omitted, provided there is nothing in the history suggestive of carcinoma or pregnancy. Patients should be warned to avoid the possibility of conception in the intervals between roentgen treatments.

Twelve of our patients received roentgen treatment, and in eight of these the chief symptom was marked anemia, the hemoglobin varying from 20 to 40 per cent. In all, the bleeding was controlled at intervals varying from one to six weeks, the tumors have shown marked reduction, and without exception the patients are in perfect health six to eighteen months after treatment.

SUMMARY OF ROENTGEN TREATMENT

Number of cases irradiated	12
Indications:	
Severe anemia	8
Large cervical myoma (poor operative risks)	2
Submucous myoma	1
Patient refused operation because of large inoperable tumor	1
Results:	
Control of bleeding	100%
Reduction in size of tumor	100%

Two obese patients were given roentgen treatment because of large cervical myomas, the excision of which would have necessitated hazardous operations. Pressure symptoms were the dominant complaints. There has been gradual regression of the tumor in both cases with corresponding decrease in the pressure symptoms, six months following irradiation.

Another patient who refused operation had a large submucous tumor, which contraindicated the use of radium. Gradual reduction of the

TABLE IV. ASSOCIATED PATHOLOGY IN OPERATIVE GROUP (180 CASES)

Cyst of corpus luteum	42	23.3%	In 44.4% of cases there was some demon- strable ova- rian lesion
Follicular ovarian cysts	8	4.4%	
Dermoid cyst of ovary	3	1.7%	
Serous cyst adenoma	1	.6%	
Pseudomucinous cystadenoma	2	1.1%	
Carcinoma of ovary	2	1.1%	
Endometriosis (ovarian)	20	11.1%	
Parovarian cyst	2	1.1%	
Chronic pelvic inflammatory disease	42	23.3%	
Hematosalpinx	2	1.1%	
Chronic appendicitis	4	2.2%	
Acute appendicitis	2	1.1%	
Ectopic pregnancy	1	0.6%	
Intrauterine pregnancy	1	0.6%	
Cervical polypi	7	3.9%	
Hemorrhoids	2	1.1%	
Pelvic relaxation sufficient to require plastic	12	6.6%	

tumor, cessation of bleeding and good general health have resulted from roentgen treatment.

The last patient in this group had a tumor filling the abdominal cavity. Operation was attempted, but widespread adhesions incident to a previous myomectomy, and the intraligamentous position of the tumor rendered hysterectomy impossible. She was given roentgen treatment two years ago; the tumor is now one-half its original size, and the patient is free from symptoms.

SURGICAL TREATMENT

The Clark Clinic has always advocated conservatism in the management of uterine myomas. Those of us who have succeeded Dr. Clark believe firmly in the wisdom of his teaching, and this applies with particular emphasis to the surgical treatment where conservation of normally functioning organs should be carried out wherever possible.

We are not in favor of vaginal hysterectomy as a routine procedure, although this operation may be ideal in the occasional patient who presents a small tumor with considerable relaxation of the pelvic floor.

TABLE V. INCIDENCE OF MALIGNANCY IN WHOLE GROUP (ES)

Sarcoma uteri	2 cases	
Carcinoma of fundus	4 cases	%
Carcinoma of ovary	2 cases	0.8%

TABLE VI. MENSTRUAL DISTURBANCES

Menorrhagia	133	52.4%
Metrorrhagia	23	9.0%
Menorrhagia and metrorrhagia	26	10.3%
Oligomenorrhea	2	0.8%
Amenorrhea	1	0.4%
No menstrual disturbance	69	27.1%

TABLE VII. OTHER SYMPTOMS

Pelvic pain	68	26.7%	} 29.4% complained of pressure symptoms
Tumor	53	20.9%	
Backache	69	27.1%	
Pelvic pressure	23	9.0%	
Frequency of urination	41	16.0%	
Sense of weight	3	1.2%	
Dysuria	5	2.0%	
Phlebitis (or pressure)	3	1.2%	}
Dysmenorrhea	26	10.3%	

Obviously vaginal myomectomy is indicated when a pedunculated tumor projects from the cervical canal. In our series only 6 patients (3.3 per cent) were suited to this form of treatment. We have been able to follow the subsequent course in only three of these, and there has been no recurrence of bleeding.

Abdominal myomectomy is unquestionably the ideal operation in the young woman, where it is desirable to maintain her procreative as well as her menstrual functions, but we believe that it is unwise to employ this method unless the preservation of a normally functioning uterus seems assured. Unfortunately in this series relatively few tumors (6.4 per cent) were found amenable to myomectomy.

The end-results were entirely satisfactory in 82 per cent, and in only one was a subsequent hysterectomy necessary. Pregnancy has occurred in none of the eight patients in whom this possibility was conserved.

If hysterectomy is decided upon, two questions at once arise: First, shall the hysterectomy be complete or partial, and second, what shall be the disposition of the ovaries? We realize that the first of these questions is controversial, but we believe that, with few exceptions, supravaginal amputation is the operation of choice. Reports from several clinics indicate that total hysterectomy is not attended by increased mortality or morbidity, but these results do not apply to the operation as performed by the majority of surgeons.

TABLE VIII. TYPES OF DEGENERATION OF TUMORS IN OPERATIVE GROUP (180 CASES)

	2	1.1%
regeneration	34	19.0%
Calcareous degeneration	18	10.0%
Cystic and calcareous degeneration	6	2.2%
Hyaline degeneration	2	1.1%
Edema	2	1.1%
Liquefaction	1	0.6%
Carneous or red degeneration	4	3.3%
	69	38.4%

TABLE IX. MENOPAUSAL SYMPTOMS

	NONE	MILD	MODERATE	SEVERE
Ablation of ovaries	7.7%	55.7%	9.6%	26.9%
Conservation of ovaries	81.5%	12.5%		6.1%
Radium	31.2%	39.5%	14.6%	14.6%
X-ray		41.6%	16.6%	41.6%

TABLE X. BACKACHE

	CURED	IMPROVED	UNCHANGED
Ablation of ovaries	48.1%	25.9%	25.9%
Conservation of ovaries	50.0%	21.4%	28.5%
Radium (4 cases)	75.0%	25.0%	
Myomectomy (4 cases)		75.0%	25.0%

The fact is indisputable that carcinoma of the cervix may develop after a supravaginal hysterectomy, but this is comparatively rare, and we are convinced that the increased mortality and morbidity attendant upon the universal adoption of total hysterectomy would far exceed

TABLE XI. RESULT OF ROENTGEN IRRADIATION IN ANEMIC PATIENTS

SIZE OF TUMOR	EFFECT OF X-RAY ON BLEEDING	POST X-RAY SIZE OF TUMOR	MENOPAUSAL SYMPTOMS	GENERAL HEALTH
3 months	No bleeding	50% reduction	Severe	Excellent
3½ months	No bleeding	Barely palpable	Mild	Excellent
2½ months	No bleeding	Barely palpable	Moderate	Excellent
3½ months	No bleeding		Severe	Excellent
5 months	No bleeding	Marked reduction	Mild	Excellent
4 months	No bleeding	Reduced to 3 months	Severe	Excellent
4½ months	No bleeding	Reduced to 3 months	Mild	Excellent
4½ months	Occasional slight spotting	Barely palpable	Severe	Excellent

Results based on 6 to 18 months' observation.

that incident to subsequent carcinoma of the cervical stump. The incidence of carcinoma can be largely eliminated by cauterization or repair of the diseased cervix as a preliminary step to the supravaginal operation. This is substantiated by the recent statements of Pemberton and Smith that of 669 patients with carcinoma of the cervix none had had a previous cauterization and that in none of 1408 patients whose cervixes had been cauterized has carcinoma been known to develop. Graves states that in 5000 cases of cervical repair, only 4 patients have been known to develop carcinoma, an incidence of less than one tenth of one per cent.

As regards the disposition of the ovaries, our clinic has always advocated conservation when possible, for by so doing distressing menopausal symptoms do not develop or are moderate in severity.

In this series one or both ovaries were conserved in 60.8 per cent. Of these 81.5 per cent did not complain of menopausal symptoms—and in only 6.1 per cent were these symptoms severe. Contrast this with the incidence of 26.9 per cent of severe menopausal symptoms following bilateral oophorectomy.

Ovarian conservation is also important from the standpoint of the preservation of regular menstruation in young women who require a supravaginal hysterectomy. In patients under forty years of age we attempt to conserve sufficient endometrium to permit of regular, though lessened, menstruation. Following this plan regular menstruation has occurred in 17.6 per cent of the patients under menopausal age; in none of these have menopausal symptoms developed, and their general health has been excellent. These results tend to confirm our belief that a complementary relationship exists between the functional activity of the ovaries and the endometrium, and that the maintenance of this relationship promotes the well-being of the individual.

RESULTS IN HYSTERECTOMY GROUP

The results following hysterectomy were satisfactory in 92.5 per cent. Lumbar or sacral backache was noted in 55 cases before operation. Of these patients 49.1 per cent were entirely relieved, 23.6 per cent improved, and in 27.2 per cent there was no improvement so far as backache was concerned.

MORTALITY

In the entire series four deaths occurred, or a total mortality of 1.57 per cent. There were no deaths after irradiation, thus making the operative mortality 2.15 per cent.

Pulmonary embolism was the cause of death in three patients, and autopsy proved the fourth to be due to massive atelectasis of the lower lobes of both lungs, associated with chronic myocarditis. The deaths from embolus occurred on the sixth, eleventh and fourteenth postopera-

tive days respectively. Each of these patients had large tumors, and in two, hysterectomy was extremely difficult because of their intraligamentous position.

SUMMARY

Two hundred and fifty-four cases of myoma uteri are reviewed from the standpoint of treatment and end-results.

Radium was employed in 21.3 per cent with satisfactory results in 93.7 per cent.

Roentgen irradiation was the method of choice in 4.7 per cent, and the results were uniformly good.

Seventy-three and two-tenths per cent were operated upon. The end-results in this group were entirely satisfactory in 92.5 per cent.

There were no deaths following irradiation.

The operative mortality was 2.15 per cent.

CONCLUSIONS

There is no lesion in the pelvis which requires more careful individualization in the choice of treatment than a uterine myoma. Each patient presents a different problem, and the appropriate treatment can be chosen only after judicious consideration of all factors concerned.

Irradiation is not to be looked upon as a competitor of surgery; each has its place in the treatment of myomas; the indications for each method are sharply defined, and the use of one to the exclusion of the other is not to the best interest of the patient.

REFERENCES

- (1) *Clark, J. G., and Block, F.*: AM. J. OBST. & GYNEC. 10: 560, 1925. (2) *Graves, W. P.*: Gynecology, Philadelphia, 1928, ed. four, page 401, W. B. Saunders Co. (3) *Kelly, H. A.*: Gynecology, New York, 1928, ed. one, page 622, D. Appleton & Co. (4) *Keene, F. E., and Block, F.*: AM. J. OBST. & GYNEC. 17: 848, 1929. (5) *Pemberton, F. A., and Smith, G. Van S.*: AM. J. OBST. & GYNEC. 17: 165, 1929.

133 SOUTH THIRTY-SIXTH STREET.

(For discussion, see page 266.)

McSwiney, B. A.: Is Quinine Induction of Labor Absolutely Harmless? J. Obst. & Gynec. Brit. Emp. 36: 90, 1929.

This is a report of 2 cases in which 30 gr. of quinine was used to induce labor. In each case the fetus did not survive. The first, delivered easily with forceps since fetal heart sounds could not be heard, was born dead, and the second, delivered spontaneously, died 21 hours after birth. No postmortems were obtained. The author wonders whether occasional cases exist which have an idiosyncrasy for quinine and for which the usual dose of 30 gr. is dangerous.

FRANK SPIELMAN.

FUNDAMENTAL BIOCHEMICAL FACTORS IN PREGNANCY*

BY MAX TRUMPER, PH.D., PHILADELPHIA, PA.

AT THE present time it is generally recognized that the metabolism of a pregnant woman is different from that of a nonpregnant woman. If one accepts the premise that pregnancy is a physiologic process, one must realize that such metabolic alterations are likewise to be considered physiologic. It is my purpose to discuss briefly the fundamental biochemical alterations during pregnancy and to attempt to show how variations beyond these physiologic limits may lead to serious complications.

Protein Metabolism.—The normal adult of constant weight is in a state of nitrogen equilibrium, that is, the nitrogen or protein intake is balanced by the nitrogen output. An insight into the terminal stages of protein metabolism may be gained by examining the nitrogenous constituents of the blood. The most important of these are: urea nitrogen 12 to 15 mg. per cent; uric acid 2 to 3.5 mg. per cent; creatinine 1 to 2.0 mg. per cent; amino acids 5 to 8.0 mg. per cent; ammonia nitrogen 0.1 to 0.2 mg. per cent, and other constituents of less importance. In addition there is the undetermined nitrogen fraction which in the opinion of some authorities is of prime importance in certain abnormal conditions. *The sum total of these nitrogen compounds comprises what is termed the total nonprotein nitrogen, which ranges normally from 25 to 35 mg. per 100 c.c. of blood.*

The end-products of nitrogen metabolism are represented by the appearance of these same substances in the urine, but of course in different concentrations.

Protein Requirements in Pregnancy.—The pregnant woman, in contradistinction to the nonpregnant woman, is not in nitrogen equilibrium, her nitrogen output being less than her intake. In other words she is in a state of positive nitrogen balance. The reason for this is apparent from the fact that the pregnant woman must satisfy the requirements of the growing fetus in addition to those of her growing body. Near the end of pregnancy this positive balance is reduced since the demand for nitrogen by the fetus is diminished.

The intermediate protein metabolism as evidenced by extensive studies of the nitrogenous constituents of the blood is but little altered during pregnancy. *There is a slight diminution in urea nitrogen, balanced by a slight increase in amino acids and ammonia nitrogen. There is also a constant but slight increase in uric acid. A very important variation*

*Read before The Obstetrical Society of Philadelphia, Feb. 6, 1930.

from the normal is encountered in a study of the plasma proteins. Normally the ratio of albumin to globulin is about three and one-half to one, fibrinogen existing in very small amount. During pregnancy, beginning about the third month there is a diminution in plasma proteins which is due almost entirely to a decrease in the albumin fraction. This results in a relative increase of globulin and fibrinogen, the latter being increased much more than the former.

Urinary findings with regard to protein metabolism in pregnancy differ but slightly from these findings in the nonpregnant state. There is a slight decrease in the output of urea and a corresponding rise in amino acids and ammonia.

Fat Metabolism.—Alterations in fat metabolism occur during pregnancy but the significance of these changes is difficult to determine. *It is definitely established that there is an increase in the concentration of cholesterol and other lipoids as well as of total fat in the blood.* Too little is known concerning the metabolism of cholesterol to enable us to interpret these findings to practical advantage. *One very important deviation from normal fat metabolism is generally recognized as occurring in pregnancy, namely a distinct tendency toward a state of mild ketosis.* This is evidenced by the excretion of acetone bodies as a result of diets which would not produce this result in the nonpregnant woman. This will be discussed in greater detail in the consideration of acid-base equilibrium.

Carbohydrate Metabolism.—Obviously under the conditions of normal pregnancy, providing as it must for the constant growth of the fetus, a distinct alteration in the carbohydrate requirement must take place. Whether or not there occurs any disturbance of carbohydrate metabolism, it is difficult to say; if it does occur, it is in all likelihood more in the nature of a quantitative than a qualitative change. We do know that in many cases there is an excretion of sugar in the urine. This occurs without any increase in the concentration of glucose in the blood, and in the opinion of most investigators is due to a decrease in the renal threshold for glucose rather than to any actual disturbance in carbohydrate metabolism. In other words the permeability of the kidneys is increased, constituting a state analogous to that of renal diabetes. One must remember that not all sugar found in the urine is glucose. Particularly in the later months of pregnancy and during lactation, lactose is apt to be excreted in the urine. Most observers report an increase in the lactic acid content of the blood and urine. This is evidence of some interference with the complete combustion or resynthesis of glycogen in the tissues, but the exact mechanism underlying this increase is debatable.

Acid-Base Equilibrium.—There is a definite tendency toward a mild acidosis in pregnancy, beginning in the early months and persisting throughout. This acidosis is in all probability a compensated one, the

actual H-ion concentration of the blood changing only in the last weeks of pregnancy. Therefore the statement may be made that normal pregnancy is associated with a state of relative and not actual acidosis. This state is evidenced by the following laboratory findings: a decrease in the alveolar CO_2 tension, decrease in the CO_2 combining power of blood plasma, increase in the excretion of lactic acid and ammonia in the urine and by the elimination of acetone bodies. The cause of this acidotic tendency is not definitely known. Most investigators attribute it to a depletion of the alkali reserve incident to the increased production of acetone bodies and lactic acid.

Calcium Metabolism.—It has long been recognized that the pregnant state is associated with some alteration in calcium metabolism. This has been emphasized particularly because of the association of osteomalacia and tetany with pregnancy. This relationship has been exaggerated but it nevertheless is a factor of importance. During the twenty-eighth week the fetus contains only about $5\frac{1}{2}$ gm. of calcium. At the fortieth week there are 30.51 gm. of calcium. As pointed out by Hess, the loss of 5 gm. from the bones of an adult to build up the fetal skeleton could not possibly cause osteomalacia which usually begins before the seventh month of pregnancy. This effect is strongly suggestive of some endocrine action. It is of interest to note that Aub found the calcium balance in early and late pregnancy to be practically identical with that of the nonpregnant state, when maintained on low calcium intake.

The serum calcium tends to diminish as pregnancy progresses, this diminution being very rarely beyond the lower limit of normal. This finding, in the light of modern knowledge concerning calcium metabolism is strongly suggestive of a condition of hypofunction of the parathyroids, which may be associated with the hyperfunction of the thyroid which exists during pregnancy. The susceptibility to tetany likewise points toward this premise. However, it is believed at present that osteomalacia is more frequently associated with hyperfunction of the parathyroids than with hypofunction. These conflicting facts are difficult to reconcile. One must remember that the subject of calcium metabolism is an extremely intricate one and that the complete story may not be told by the level of serum calcium. The partition of calcium into diffusible and nondiffusible fractions is perhaps of more importance than the absolute level of calcium in the blood, since the ratio between these two fractions affords an insight into the distribution of physiologically active calcium in the tissues. Investigation in this direction is needed to throw more light upon the subject.

Basal Metabolism and Endocrines.—The basal metabolism increases gradually during the latter half of pregnancy. The average basal metabolic rate at term being approximately plus 20 per cent. This increased metabolism is not accounted for by the increase in weight

and must represent an endocrine action. The hypophysis is hypertrophied which increases metabolism. The other internal secretions capable of producing this metabolic alteration are thyroxin and adrenalin.

Water and Sodium Chloride Balance.—It seems well established that blood volume in the later months of pregnancy is increased. This increase is due to an increase in plasma volume and is associated with a corresponding decrease in specific gravity and in the percentage of hemoglobin and red cells. The serum proteins are likewise diluted in addition to the actual diminution in serum albumin. There is no unanimity of opinion as to the actual volume of blood in pregnancy. Blood studies on sodium chloride have been disappointing and are of no diagnostic value. We do not as yet understand the factors concerning the salt and water balance in pregnancy.

ECLAMPSIA

Biochemical studies in eclampsia have thrown but little light upon this condition. It is remarkable that with all the methods of study at our disposal at the present time, a disorder like eclampsia, characterized by severe, indeed fulminating clinical manifestations, should reveal such slight metabolic alteration.

Opinion is divided with regard to the condition of protein metabolism in eclampsia. The belief of the majority of investigators may be summed up as follows: The total nonprotein nitrogen, urea nitrogen, and creatinine are but slightly affected; uric acid is increased to a moderate degree; amino acids and ammonia are likewise increased above normal limits. None of these changes can in any way be considered of fundamental importance in throwing light upon the mechanisms concerned. The only factor which may perhaps be of significance is the undetermined nitrogen fraction. In many cases of eclampsia this is remarkably increased. However, in other cases it is within the normal limits and conversely in clinical conditions other than eclampsia it may be increased with no attending symptoms.

Carbohydrate.—The question of carbohydrate metabolism in eclampsia has been intensively investigated. It is curious that opinion can be divided concerning so absolute a factor as the level of blood sugar. However, it is about this very point that discussion centers. Titus and his followers maintain their belief in the constant occurrence of hypoglycemia during eclampsia and insist upon this factor as of fundamental importance. On the other hand Stander and his school just as firmly insist that the blood sugar in eclampsia, if altered at all, is increased. The majority of authors seem to adhere to the latter opinion. However it seems to me that the nutrition of the patient and the severity of the symptoms both prior to and during the stay in the

hospital have a distinct bearing upon the amount of glycogen reserve and upon the level of blood sugar.

Acid-Base Equilibrium.—As was previously stated during normal pregnancy there is a compensated acidosis. In eclampsia the acidosis becomes uncompensated, there being a shift in H-ion concentration of the blood toward the acid side. However this state of acidosis in itself cannot be considered a primary factor in the production of this condition since we all know that acidosis may be marked in other clinical states entirely dissimilar to eclampsia.

Calcium.—The majority of reports concerning serum calcium in eclampsia indicate that it is decreased below the level normally found during pregnancy. However this finding cannot in itself be considered of great significance since the diminution is not marked and the symptoms are unlike those ordinarily associated with slight reduction in serum calcium. As emphasized before it must be remembered that the level of serum calcium is not always a true index of the state of calcium metabolism. One must take into consideration the ratio of the diffusible to the nondiffusible and of the ionized to the nonionized fractions before any definite conclusion can be arrived at. As shown by several workers there may exist a very definite disturbance in calcium metabolism, with serious clinical manifestations yet with no change in the level of total serum calcium. The importance of inorganic metabolism in physiology is gradually coming into recognition. As our knowledge in this field increases we come to appreciate more deeply the intricate and delicate interrelationships between the metabolism of inorganic elements and of organic substances. In this connection the recent work of Minot and Cutler working with Lamson makes a most valuable contribution and is a step in the right direction toward the solution of many of the problems which concern us in considering the biochemical mechanisms underlying eclampsia. These investigators found in a group of conditions characterized by acute liver damage, both experimental and clinical and including eclampsia, certain constant changes. These consisted essentially of an increase in the amount of guanidine in the blood and a diminution in the level of blood sugar. The serum calcium was unaltered. The toxic symptoms appeared to be related to the degree of guanidine retention. To my mind* the most important and significant feature of their work was the fact that the intravenous injection of calcium salts brought about prompt relief from these symptoms, at the same time causing a return of the blood sugar to normal levels. The administration of glucose brought about a return of normal blood sugar without any relief from symptoms thus indicating that the disturbance in blood sugar although an associated factor, is not the one fundamentally involved. The most

*The forms of calcium most satisfactory for intravenous use are calcium gluconate (Sandoz) and calcium chloride.

significant factor appears to be the increased concentration of guanidine. For many years the relationship between guanidine intoxication and disturbed calcium balance has been recognized. It appears from previous works as well as that of Minot and Cutler that calcium exerts its beneficial effect upon the symptoms of guanidine intoxication by some antagonistic influence which it exerts upon that substance.

Until comparatively recently our investigations of the nature of eclampsia were directed toward the study of organic metabolism. In the past few years inorganic metabolism has come to the front. Bland and Bernstein have reported on the advantages of a salt-free diet and its effects on actual loss of fluid from the tissues. Today we know that NaCl and NaHCO₃ increase edema. It appears likely that our increasing understanding of the principles underlying the metabolism of inorganic elements and their relation to the fundamental physico-chemical mechanisms operating under normal and pathologic conditions will throw more light upon certain clinical disorders, the nature of which at the present time is obscure.

921 MEDICAL ARTS BUILDING.

(For discussion, see page 272.)

Faehrmann: Creation of an Artificial Vagina Out of the Sigmoid Flexure. *Zentralbl. f. Chir.* 56: 989, 1929.

There are two prevailing methods of creating an artificial vagina: (1) out of small intestine, (2) out of the rectum. Faehrmann, in a case of vaginal aplasia in a young girl, used the sigmoid flexure. He excluded the mobile portion of the sigmoid, thus securing a blind portion of the gut, and reestablishing the continuity of the sigmoid by lateral anastomosis. Next he separated the bladder from the rectum and crowded the excluded loop of the sigmoid down into the pelvis, leading it out of the vulva. The technic is described in detail, special emphasis being laid on the preservation of the circulation of the intact and resected portions of the sigmoid.

SEELIG.

Gausman: The Uniting of Two Graafian Follicles. *Russk. Klin.* 11: 221, 1929.

The author studied the ovary of a girl, fifteen years old, dead from acute endocarditis. Menarche at thirteen years flows regularly, four weeks' interval and three days' duration, but had been amenorrhoeic for last four months. In a series of sections, he found four places where two follicles were united to each other. At one place the granulosa of a ripening follicle was seen joined to the granulosa of an adjacent small follicle. Each follicle contained an ovum with clearly visible nucleus and nucleolus. The author feels that by means of this process of uniting of two follicles finally one follicle is formed containing two ova.

ALEXANDER G. GABRIELIANZ.

A REVIEW OF THE PROGRESS IN ENDOCRINOLOGY OF INTEREST TO THE GYNECOLOGIST AND OBSTETRICIAN*

BY ROBERT T. FRANK, M.A., M.D., F.A.C.S., NEW YORK, N. Y.
(*Gynecologist to Mount Sinai Hospital*)

THE progress made in the theoretical field of endocrinology has been startling and epochal. This progress applies likewise to our methods of diagnosis. Therapeutics has not kept pace with these advances, but the future promises much.

The gynecologist and obstetrician are mainly interested in such advancements as apply more directly to their fields. Every branch of medicine has been benefited by the discovery of Banting, Best and Collip of insulin and by the practical application of this wonderful agent. The literature bearing upon insulin has already reached prodigious proportions and requires no further discussion. The parathyroid hormone, isolated in an impure state by Collip, rarely is applicable to our field except in tetany and osteomalacia, both unusual and rare diseases.

Of more immediate interest are the advances made in the study of the female sex hormone and the pituitary gland. It is upon these two phases of the subject that I shall concentrate my remarks.

Proof that menstruation is due to the female sex hormone has been given by Allen and Pratt,¹ and Corner.² These investigators showed that in castrated primates (rhesus monkeys) injection of female sex hormone and abrupt withdrawal of the same are followed by typical menstruation. The injection of the hormone brings the uterus into the condition of premenstruation or pregravidity; its withdrawal is followed by the menstrual flow. This demonstration is clear-cut and convincing.

Proof that the corpus luteum secretes two hormones has been offered by my collaborators (Gustavson, Goldberger and McQueen) and myself,³ by obtaining from the same batch of corpora lutea the female sex hormone which gave all the usual tests, as well as the nidatory hormone. The presence of this latter hormone can be demonstrated in several ways. We were able to produce loosening of the pubic ligaments in virginal guinea pigs in a period of twelve hours by injecting the aqueous extract of the corpus luteum. The female sex hormone is obtained by lipid (ether) extraction, the nidatory hormone by aqueous extraction.

Proof that the anterior pituitary lobe secretes a hormone activating the ovary has been offered by Philip Smith,⁴ with repeated implants of fresh anterior lobe, as well as by Aschheim and Zondek,⁵ who em-

*Read at the meeting of the New York Obstetrical Society, March 11, 1930.

played an extract of the anterior lobe. Implantation or injection into immature animals produces puberty, causes massive and rapid growth of follicles in the mature, and reactivates the ovaries if senility has already ensued (Steinach and Kun⁶). Thus the anterior lobe is shown to cause puberty. The work of Evans and Simpson⁷ has demonstrated that the anterior lobe secretes at least two hormones, the one producing a general somatic growth. This hormone is elaborated, according to these authors by the eosinophilic cells, while the special gonadal stimulant is supposed to be derived from the basophilic cells. By means of excessive exhibition of the gonadal anterior lobe hormone superovulation and superfetation to an astounding degree, can be brought about.

Excess excretion of the anterior lobe hormone as well as of the female sex hormone in the urine of pregnancy has been demonstrated by Aschheim and Zondek.⁸ The excess produced is amazing. As much as 10,000 M. U. per liter (a mouse unit represents the amount of female sex hormone necessary to produce full estrus in a castrated mouse) has been excreted in twenty-four hours. Because of this excess production, the urine of pregnant women has been used in all the later investigations for the isolation of the female sex hormone.

Crystalline female sex hormone was announced in August, 1929, by Doisy.⁹ Since then Butenandt of Göttingen has likewise obtained a crystalline product from the urine of pregnancy. According to newspaper reports, the original article not being available to me at the moment, Collip has obtained the same crystalline product from the placenta. Butenandt believes that the hormone will prove to be related to the stearates. My collaborator, Gustavson, more than a year ago, found evidence pointing to the fact that the hormone is a gamma lactone. We may soon expect to obtain the chemical formula as well as the structure of this important hormone.

The widespread presence of the female sex hormone should be kept in mind. In small quantities it has been demonstrated in yeast (Fellner,¹⁰ Frank and Goldberger¹¹); in greater quantity it can be found in the ovaries as well as in other portions of many plants (Loewe¹²). In mammals it has been demonstrated in the follicle fluid (Frank,¹³ Allen and Doisy¹⁴); in the corpus luteum (Aschner,¹⁵ Fellner¹⁶); in the placenta (Iscovesco¹⁷); in the blood (Loewe,¹⁸ Frank, Gustavson, Frank, and Weyerts¹⁹); in the urine of normal women (Loewe²⁰), as well as of pregnant women (Aschheim and Zondek⁸); in the feces (Dohrn and Faure²¹); in the bile (Gsell-Busse²²); in the blood of males and in other tissue fluids. My own hypothesis is that the female sex hormone first produced general tissue growth but later became more specialized, and finally its effect has become limited to the genital tract and the breasts. Its appearance in the bile of both sexes, as well as its appearance in the blood and urine of males, appears accounted for by absorption from the intestinal tract. Together with Goldberger I

have obtained evidence that the liver takes up the circulating female sex hormone and stores it in the gall bladder. When this viscous empties, rapid reabsorption appears to occur, with temporary flooding of the circulating blood. As the female sex hormone has a distinctly anti-masculine effect (Laqueur²³), the *raison d'être* for this protective mechanism is accounted for. The average potato, for example contains from 1 to 2 mouse units of female sex hormone.

Three types of menstruation. The work of Gebhard,²⁴ Schröder,²⁵ Heape²⁶ and Corner,²⁷ has shown that menstruation takes place through the endometrium under different conditions.

The commonest form is that of Schröder in which a marked pregravid reaction occurs, the endometrium being divisible into three layers, a superficial compact layer, a spongy layer, these two being called the functional layers, and an unchanged narrow basilar layer. At the time of menstruation the functional layers are cast off, and the narrow, exposed basilar layer alone remains. Through this open wound which resembles the uterine lining postpartum, the blood sickens.

Gebhard showed that in a certain number of cases, although the functional pregravid changes occur, the hemorrhage takes place by diapedesis as well as the formation of superficial hematomata without great loss of substance.

Heape in 1899, as well as Corner more recently, called attention to the fact that in the macacus and *Simnephithicus entellus* type of monkeys, menstruation may occur through an unchanged endometrium by diapedesis.

How to account for these three mechanisms, I am unable to state at present.

DIAGNOSIS

Aschheim and Zondek have utilized the excess excretion of anterior lobe hormone in the urine to devise a very accurate test for pregnancy. Small amounts of untreated urine are injected in five small quantities into immature mice or rats. In one hundred hours, if pregnancy exists, these animals mature, and blood spots, readily recognizable macroscopically, are found in the ovaries. This test gives 95 per cent of positive results macroscopically. Its sole drawback is that one hundred hours must elapse before the readings can be made. Moreover the demand for immature mice exceeds the available supply.

Estimation of the amount of female sex hormone circulating in the blood is now feasible (Frank and Goldberger²⁸). By this means the concentration present at any time in the blood can be demonstrated. This is of particular importance in evaluating functional amenorrhea, premenstrual "tension," the diagnosis of obscure tumors (fibroids vs. pregnancy), whether the fetus is alive or dead, etc. Our studies have been confirmed by Hirsh,²⁹ Mazer and Hoffman,³⁰ Siebke,³¹ and in some particulars by Janney.³²

Demonstration of the female sex hormone in the urine has been utilized by us (Frank and Goldberger³³) to determine the excretory threshold of the hormone. It appears that in a number of conditions, particularly of amenorrhea and sterility, an unduly low excretory threshold nullifies an otherwise normal production of the hormone. Further studies along these lines are being pursued by us. These investigations demonstrate that the effect to be expected from ovarian action, as well as from oötherapy, may be nullified by this abnormal renal permeability.

I desire once more to emphasize that today the proper evaluation of an endocrine condition entails much laborious investigation.

The pituitary function is difficult to estimate. As aids, x-ray pictures of the sella turcica, the sugar tolerance of the patient, the development of the acra must be taken into consideration.

Thyroid function can be readily estimated by the basal metabolism, but some thyroid symptoms are not fully accounted for by the rate of metabolic exchange.

Adrenal function is most difficult to estimate. Disturbances of this gland may show themselves by pigmentation and hirsutes. Diminished function is recognized under the general symptoms of Addison's disease.

The adrenal medulla apparently, to some extent, governs the blood pressure, but much obscurity yet obtains.

Parathyroid function is recognized by the level of the circulating calcium as well as by the response of nerves to stimulation.

The pancreatic function is readily studied by the blood-sugar level and the permeability of the kidneys to dextrose.

TREATMENT

The purely mechanistic treatment of sterility and amenorrhea has been exaggerated. By this I do not desire to suggest that, particularly in sterility, mechanical permeability is not of utmost importance, but in the absence of previous infection this etiologic factor rarely obtains. Therefore, the present tendency to overlook evident and striking endocrine disturbances cannot be too strongly emphasized.

Functional sterility is of frequent occurrence in the sterile group. Infantilism, obesity, overt and serious endocrine diseases, such as acromegaly, Froehlich's syndrome, and serious systemic diseases are often at fault. Amenorrheas fall into two groups. The first and most serious shows absence of cyclical function. The second shows greatly diminished ovarian cyclical function or undue renal permeability to the hormone. Many amenorrheic patients are also obese. Without the female sex hormone test of the blood and the urine, I am unable to distinguish between these two groups, the prognosis and treatment of which differ greatly. Obesities require slow and careful reduction of weight. In the presence of cyclical ovarian function "stimulating"

radiation of the ovaries is indicated. It is, however, strongly contra-indicated in the amenorrheas showing no cyclical ovarian activity.

Menorrhagia and metrorrhagia of functional origin are difficult to interpret unless evident endocrine diseases, blood dyscrasias, or other recognizable causes (such as fibromyomas, malignancies, subinvolution, etc.) can be determined and in the absence of such causes may be due to overfunction of the ovaries. We have been able to demonstrate such excess function in only a small percentage of cases. The value of this demonstration is, therefore, almost negligible. This is of little importance, as the treatment of both organic and functional metrorrhagia and menorrhagia is identical. As heretofore, certain drugs may prove of value. Repeated curettages, ovarian irradiation, or intrauterine radium, rarely, resection of the ovaries may be employed.

Menopause symptoms resist treatment to a great degree. The vaginal administration of female sex hormone affords relief in a limited number of instances.

Organotherapy. In spite of the advances in physiology, organotherapy continues to prove disappointing. The available female sex hormone is of little use. All the samples titred by me have continued to show but little and very transient activity. The hypodermic preparations frequently produce unpleasant local reactions. Some of them also cause systemic symptoms of disturbing nature. None of the anterior lobe preparations are as yet suitable for human use. From what we have learned in the past, I feel more and more that our future hopes must be concentrated upon the anterior lobe preparations, which are the motors of the ovaries, as Zondek and Aschheim aptly term them, rather than upon the female sex hormone which stimulates the tubular tract without influencing the ovaries themselves.

Our present methods of therapy, therefore, have not changed greatly. Our hopes should, therefore, be pinned upon general measures, remembering that of the organotherapeutic preparations thyroid extract, insulin and parathyroid hormones are our mainstays. For special purposes, adrenalin and pituitrin are indicated.

REFERENCES

- (1) Pratt, J. P., and Allen, E.: J. A. M. A. 86: 1964, 1926. (2) Corner, G. W.: J. A. M. A. 89: 1838, 1927. (3) Frank, R. T., Gustavson, R. G., McQueen, H., and Goldberger, M. A.: Am. J. Physiol. 90: 727, 1929. (4) Smith, P.: Am. J. Physiol. 80: 114, 1927. (5) Zondek, B., and Aschheim, S.: Klin. Wehnschr. 6: 248, 1927. (6) Steinach, E., and Kun, H.: Med. Klin. 24: 524, 1928. (7) Evans, H. M., and Simpson, M. E.: J. A. M. A. 91: 1337, 1928. (8) Aschheim, S., and Zondek, B.: Klin. Wehnschr. 6: 1322, 1927. (9) Doisy, E. A.: Tr. Internat. Physiol. Congress, 1929, Boston. (10) Fellner, O. O.: Pflüger's Arch. f. d. ges. Physiol. 189: 199, 1921. (11) Frank, R. T., and Goldberger, M. A.: See Frank, The Female Sex Hormone, 1929, Springfield, Thomas. (12) Loewe, S.: Akademie d. Wissenschaften in Wien., Oct. 21, 1926. (13) Frank, R. T.: J. A. M. A. 78: 181, 1922. (14) Allen, E., and Doisy, E. A.: J. A. M. A. 81: 819, 1923. (15) Aschner, B.: Arch. f. Gynäk. 99: 534, 1913. (16) Fellner, O. O.: Zentralbl. f. allg. Path. 23: 673, 1912. (17) Iscovesco, H.: Compt. rend. Soc. de biol. 72: 858, 1912. (18) Loewe, S.: Klin. Wehnschr. 4: 1407, 1925.

- (19) Frank, R. T., and Frank, M. L., Gustavson, R. G., and Weyerts, W. W.: J. A. M. A. 85: 510, 1925. (20) Loewe, S., and Lange, F.: Klin. Wehnschr. 5: 1038, 1926. (21) Dohrn, M., and Faure, W.: Klin. Wehnschr. 7: 943, 1927. (22) Gsell-Busse, M. A.: Klin. Wehnschr. 7: 1606, 1928. (23) Laqueur, E., Hart, P. C., and de Jongh, S. E.: Deutsche med. Wehnschr. 52: 1247, 1926. (24) Gebhard, C.: Pathologische Anatomieder Sexualorgane, Leipzig, 1899, S. Hirzel. (25) Schröder, R.: Monatschr. f. Geburtsh. u. Gynäk. 39: 3, 1914. (26) Heape, W.: Tr. Obst. Soc., London 40: 161, 1899. (27) Corner, G. W.: J. A. M. A. 89: 1838, 1927. (28) Frank, R. T., and Goldberger, M. A.: J. A. M. A. 87: 1719, 1926. (29) Hirsch, H.: Arch. f. Gynäk. 133: 173, 1928. (30) Mazer, C., and Hoffman, J.: AM. J. OBST. & GYNEC. 17: 186, 1929. (31) Siebke, H.: Zentrabl. f. Gynäk. 39: 2450, 1929. (32) Janney, J. C.: Arch. of Surg. 18: 1241, 1929. (33) Frank, R. T., and Goldberger, M. A.: In press, J. A. M. A.

10 EAST EIGHTY-FIFTH STREET.

(For discussion, see page 265.)

FRANK TEST FOR THE FEMALE SEX HORMONE

A REPORT OF A STUDY MADE AT THE WOMAN'S HOSPITAL

BY HELEN W. SPENCER, M.D., NEW YORK, N. Y.

(Clinical Assistant, Woman's Hospital)

ROBERT T. FRANK in a recent monograph describes substantially the following characteristics of what he calls the female sex hormone. It is abundantly present in follicular fluid, in the corpus luteum, and in placental tissue. When injected into spayed rodents it will induce estrus. It can be demonstrated in the blood of normal women from one to five days before menstruation. During the menstrual period it disappears, or cannot be demonstrated; it is again demonstrable in the week before the next menstrual flow. It can be demonstrated in the blood of some women with amenorrhea: in these cases the occurrence of the hormone may follow a definite cycle, or it may occur irregularly. In other cases of amenorrhea, presence of the hormone cannot be demonstrated. In cases where, due to congenital anomalies, the sex of the individual is undetermined, demonstration of this hormone's presence is valuable, since a positive test implies ovarian function.

Demonstration of this hormone, or of its absence, seemed applicable not only to cases of amenorrhea, but also to those cases of sterility apparently due to functional endocrine disorders not accompanied by amenorrhea. With this idea in mind, we used Frank's test for the hormone on a series of 21 cases selected at the clinic of the Woman's Hospital, at the direction of the chief surgeon.

Technic.—There are 40 c.c. of blood withdrawn from a vein and mixed with 30 gm. of anhydrous sodium sulphate until dry. The mixture is then pulverized and for ten minutes shaken with 125 c.c. of ether. This mixture is allowed to settle; then the ether is decanted into an evaporating dish. The sludge is again shaken with 75 c.c. of fresh ether; the ether is again allowed to settle; the ether is de-

Thanks are due Dr. Frank and his assistant Dr. Goldberger for their kindness in permitting me to learn the technic by observation of the methods used in their laboratory. Their advice was of the greatest assistance.

canted and added to that previously decanted. After the ether has evaporated, the residue is dissolved in 2 c.c. of sterile water and injected, by divided doses, into a female mouse that has been spayed at least ten days previously. Vaginal smears from the mouse are examined in twenty-four, forty-eight, and sixty hours. A negative smear shows only mucus and polynuclear leucocytes; a strongly positive smear shows only cornified epithelial cells; intermediate stages show nucleated epithelial cells in varying numbers, as well as cornified cells.

Of the 21 cases studied, 12 patients complained chiefly of sterility. Each of these cases had been previously examined for pelvic abnormalities. The fallopian tubes had been insufflated by Rubin's method and found patent (except in the case of congenital absence of the vagina). In each case the husband had been examined by a urologist and pronounced fertile. In other words, no definite cause for the sterility other than a possible endocrine disturbance could be demonstrated.

Some of the cases studied had scanty or irregular menstruation. Others had amenorrhea for varying lengths of time. One had an excessive menstrual flow. In the cases of amenorrhea the test was repeated at intervals of about a week to determine whether there was a cycle. When the occurrence of menstruation was predictable, a specimen of blood was tested in the week preceding the expected flow.

Two normal women who had borne children and several pregnant women were tested as controls. The blood of the normal women gave definitely positive reactions preceding the menstrual flow and negative reactions following it (Cases 16 and 17). The pregnant patients, who were in the sixth month or later, invariably gave strongly positive reactions.

In the sterility cases, even when menstruation was regular, there was a great variety in the results obtained, as evidenced by the following records.

CASE 1.—Aged twenty-five. Chief complaint: amenorrhea two months, last regular period April 19, 1928. Blood taken June 12, 1928 was strongly positive.

The strongly positive reaction in this case could mean that menstruation was about to occur, or that the patient was pregnant. Menstruation did not occur, and pelvic examination later showed a definitely pregnant uterus.

CASE 2.—Pregnant seven months. Blood hormone test strongly positive.

CASE 3.—Pregnant six months. Blood hormone test strongly positive.

CASE 4.—Pregnant eight months. Blood hormone test strongly positive.

This agrees with Dr. Frank's finding that the test is positive in the latter months of pregnancy.

CASE 5.—Aged twenty-five. Chief complaint: sterility. Married three years. Menses irregular with occasional periods of amenorrhea. Blood taken June 28, 1928, and July 13 and 18, 1928, was negative. Menstruated July 25, 1928. Blood taken Aug. 1, 1928, was doubtful. Six doses of stimulating x-ray were given at weekly intervals, beginning Aug. 8, 1928. Blood taken Oct. 31, 1928, was positive. Menstruated Nov. 2, 1928.

This case shows a slightly positive reaction both preceding and following a

scanty menstrual period. The premenstrual reaction was stronger after the course of x-ray treatment although the flow was not increased.

CASE 6.—Aged twenty-nine. Chief complaint: secondary sterility, scanty menses. Married ten years. She had an induced abortion at three months ten years ago. Blood taken June 27 and July 2, 1928, was negative. Menstruated July 6, 1928. Blood taken July 18, 1928, was positive and July 25, 1928, was negative.

This patient, fertile ten years ago, with regular although scanty menses, gives a positive reaction following menstruation rather than preceding it. It may be that this reversed relation of menstruation to the appearance of the hormone in the blood is a cause of sterility in some women.

CASE 7.—Aged twenty-five. Chief complaint: secondary sterility, irregular menses. She had three spontaneous abortions at three months, the last one in 1925. She has marked hirsutes. Blood taken July 12, 1928, was negative. Menstruated July 14, 1928. Blood taken July 18 and 25, 1928, was negative. Menstruated Sept. 5, 1928. Blood taken Oct. 11, 1928, was negative.

The test is negative both before and after menstruation. It is probable that the hormone is in the blood in insufficient quantity to give a reaction when tested. Since she has been pregnant, although unable to carry beyond three months, it is possible that the hormone may have been present in larger quantities, yet insufficient to permit further development of the fetus.

CASE 8.—Aged thirty. Chief complaint: primary sterility, amenorrhea from February to June, 1928. Menstruated June 26, 1928. Next period expected July 12, 1928. Blood taken July 18, 1928, was negative. Menstruation did not occur.

A course of 6 doses of stimulating x-ray was given, after which she menstruated more regularly. Further blood tests were not obtained.

CASE 9.—Aged twenty-nine. Chief complaint: primary sterility, amenorrhea for the past five years. Blood taken Aug. 1, 1928, was positive, Aug. 6 and 13 was negative, Aug. 21 was positive.

A definite twenty-one day cycle is present although not followed by menstruation. This may be considered a subthreshold type in which the hormone is present but insufficient to be followed by menstruation.

CASE 10.—Aged twenty-seven. Chief complaint: primary sterility. Irregular, scanty menses. Blood taken Oct. 3, 1928, gave a positive reaction. Menstruated Oct. 8, 1928. Blood taken Oct. 29 and Nov. 5, 1928, was negative. Menstruation was expected Nov. 10, 1928, but did not occur. Blood taken Nov. 10, 1928, was negative.

Blood taken five days preceding menstruation gave a positive reaction, but that taken four weeks later, preceding the time menstruation was expected, gave a negative reaction. Menstruation did not occur following this test. This indicates the relation between the appearance of the hormone and menstruation described by Dr. Frank, which has not been apparent in most of these cases.

CASE 11.—Aged thirty-eight. Chief complaint: amenorrhea for four months. Blood taken Oct. 22 and 29, 1928, was negative. Menstruated Nov. 4, 1928. Blood taken Dec. 3, 1928, was negative.

The first blood test was negative seven days before menstruation. If the test had been repeated before the menstrual period, it might have been positive, although it was again negative Dec. 3, 1928, two days before the next period which began Dec. 5, 1928. The negative test in conjunction with the apparent senility of the pelvic organs favored a diagnosis of early menopause in this case.

CASE 12.—Aged twenty-seven. Chief complaint: primary sterility. Married four years. Menses regular, normal. Last menstruation Nov. 1, 1928. Blood taken Nov. 27, 1928, was negative. Menstruation did not occur at the expected time.

Pelvic examination a few weeks later showed this patient to be pregnant. The test was negative four weeks after the last menstruation. Positive tests are expected later in pregnancy. During the first three months of pregnancy the test is unreliable although it may be suggestive as in Case 1, which gave a strongly positive reaction at eight weeks.

CASE 13.—Aged thirty-one. Chief complaint: amenorrhea for five years. Menses always irregular. Married eleven years. No pregnancies. Blood taken Nov. 26, 1928, was negative.

Further tests were refused.

CASE 14.—Aged thirty-three. Chief complaint: primary sterility, menorrhagia. Married five years. Blood taken Jan. 2, 1929, was negative. Menstruated Jan. 4, 1929, profuse. Blood taken Jan. 28, 1929, was negative. Menstruated Jan. 29, 1929, profuse. Blood taken Feb. 4, 1929, was negative.

Although menstruation was regular and profuse, the hormone could not be demonstrated in the blood either preceding or following the period. A few weeks later the uterus was curetted to determine the cause of the menorrhagia. The curettings showed only a moderate hyperplasia. The menstrual flow has been normal since the operation but pregnancy has not occurred. Postcoital examination of vaginal and cervical secretions showed no abnormal physical or chemical inhibitions of the spermatozoa. Since the menstrual function is now normal, although formerly profuse, there seems to be no relation between the demonstrations of the hormone and the occurrence of menstruation.

CASE 15.—Aged thirty. Chief complaint: amenorrhea for seven years following a normal pregnancy. Blood taken Jan. 14, 1929, was negative; Jan. 21, 1929, was doubtful; Jan. 28 and Feb. 4, 1929, was negative.

The hormone is present but in subthreshold amounts. Stimulating x-ray treatment was tried with no improvement.

CASE 16.—Aged twenty-nine. No complaints. Menses regular, normal. Normal pregnancy two years ago. Blood taken March 21, 1929, was negative (only 30 c.c. of blood were obtained). Menstruated March 25, 1929. Blood taken April 16, 1929, was negative; April 22, 1929, was positive. Menstruated April 24, 1929.

In this case, a normal control, the blood was positive two days preceding the menstrual period when a full 40 c.c. were tested. At the first attempt, four days preceding a period, only 30 c.c. of blood were obtained, which was insufficient to produce a positive reaction.

CASE 17.—Aged twenty-four. Chief complaint: total amenorrhea, dyspareunia. Married five months. Examination showed total absence of vagina and uterus. The secondary sex characteristics were feminine, and desire apparently normal. Blood taken Feb. 14, 1929, was negative; Feb. 18, 1929, was strongly positive, and Feb. 25, 1929, was negative.

Tests were done at an interval of a few days, the first was negative, the second strongly positive, and the third negative, showing an intermittent discharge of the female sex hormone into the blood stream presumably from ovarian tissue somewhere in the body.

CASE 18.—Aged thirty-two. Chief complaint: primary sterility. Married six years. Menses regular but scanty. Blood taken Feb. 18, 25, and Mar. 4, 1929, was negative. Blood taken Mar. 11, 1929, was strongly positive. Menstruated Mar. 13, 1929.

The hormone was strongly positive in this case although menstruation was scanty. It was only demonstrable a few days before the menses occurred, although the test was repeated at weekly intervals for the month.

CASE 19.—Aged twenty-nine. Chief complaint: primary sterility, scanty menstruation. Married three years. Blood taken Feb. 1 and 25, 1929, was negative. Menstruated Feb. 28, 1929. Blood taken Mar. 1, 1929, was negative.

Although blood was taken only three days before the menstrual flow, it gave a negative reaction. This is in marked contrast to the preceding case (Case 18) which is otherwise similar.

CASE 20.—Aged twenty-three. Chief complaint: primary sterility, amenorrhea for eight months. Blood taken Mar. 4, 12, 19, and 26, 1929, was negative.

A definite insufficiency of the hormone.

CASE 21.—Aged thirty. No complaints. Two normal pregnancies, the last one in 1927. Blood taken April 15, 1929, was positive. Menstruated April 17, 1929. Blood taken April 29, 1929, was negative.

A normal reaction in a normal control, positive preceding menstruation, negative following.

SUMMARY

Frank's test for the female sex hormone in the blood was done on a series of 21 cases. Of these cases, 12 of the patients complained chiefly of sterility, with or without menstrual irregularities. Four complained of amenorrhea varying from two months to seven years in duration. Three pregnant and two normal women were tested as controls.

The blood of the normal women gave positive reactions preceding menstruation and negative reactions following it. The pregnant cases, in the sixth month or later, invariably gave strongly positive reactions. This is in accord with Dr. Frank's findings.

In the cases of sterility and amenorrhea, there was a great variation in the results obtained. There were five cases of sterility with regular menstruation. Three of these gave negative reactions to repeated tests. One later proved to be four weeks pregnant at the time the test was made. One gave a positive test preceding menstruation; another was positive only after the flow.

There were four cases of sterility with irregular menstruation. Of these, two gave negative reactions to each test; one was positive before the flow; one gave a slightly positive reaction both before and after the flow.

Of the cases of amenorrhea, one with a strongly positive reaction was eight weeks pregnant. Two had definite cycles when a positive reaction was obtained although negative at other times. One gave a slightly positive reaction on one test. Three gave negative reactions whenever tested.

Stimulating x-ray therapy was tried in three cases with slight improvement in two, but with no change in the third.

CONCLUSIONS

1. Menstruation does not necessarily occur in cases when a definite cyclic appearance of the female sex hormone can be demonstrated in the blood.

2. Menstruation may occur regularly, and even profusely, when the female sex hormone is absent or in insufficient quantity to be demonstrated in the blood.

3. If a strongly positive reaction preceding the menstrual period is accepted as the normal reaction, all but one of the cases complaining of sterility showed a definite variation from the normal, either in the strength of the reaction, its relation to the appearance of the menses, or by a negative reaction.

4. The female sex hormone in the blood is increased in amount during pregnancy.

5. Amenorrhea is, in itself, no evidence of sterility: the presence or absence of the female sex hormone in the blood may be the conclusive factor in a prognosis in such cases.

6. No definite conclusions can be drawn from so few cases; the general inferences, however, encourage further investigations along the lines indicated.

REFERENCES

Frank and Goldberger: N. Y. St. J. Med. 29: 271, 1929. *Frank, R. T.*: Surg. Gynec. Obst. 45: 189, 1927. *Frank and Gustavson*: J. A. M. A. 84: 1715, 1925. *Allen*: Am. J. Anat. 30: 297, 1922. *Long and Evans*: Mem. Univ. Calif. 6: 98, 1922. *Moench, G. L.*: AM. J. OBST. & GYNEC 13: 334, 1927. *Polak, J. O.*: Surg. Gynec. Obst. 44: 520, 1927. *Frank, R. T.*: The Female Sex Hormone, Chas. C. Thomas, 1929.

121 EAST SIXTIETH STREET.

THE "RADICAL" IN OBSTETRICS*

BY JAMES W. DUNCAN, M.D., MONTREAL, QUEBEC

(From the Service of the Royal Victoria Maternity Hospital)

"THE estimate of a man's future usefulness to the State, may more often than not be measured by the manner of his birth."

Today one may divide the obstetric workers into three camps—the abolitionists, the moderates, and the conservatives. Of the three, which is the "radical"? How should one define the term? In our own translation the word extremist is a fair substitute. The enthusiast in each of these groups will point the finger of criticism at the other. Two of the groups must be at fault and being in error, constitute a grave danger.

Fetal death is a great catastrophe, but how much worse is later mental deficiency. Forceps and breech extraction are the two most frequent factors in the production of these two conditions; the pelvic canal, however, is a good third.

The doctrine of the abolitionist, of the whole or part of labor, more particularly the second stage, we know too well and may thus avoid recapitulating.

*Read at a meeting of the Brooklyn Gynecological Society, March 7, 1930.

Ultraconservatists wait for definite signals of maternal or fetal distress. The question arises: Do they frequently hesitate just a moment too long?

Recently we have been entertained by a published statement to the effect that the safest place for a woman to give birth to her baby is at home under the care of a midwife. One wonders if the writer of this ingenuous article realizes how free the midwife becomes after passing the responsibility on to the doctor or, as more frequently occurs, to the hospital.

Further discussion of this matter would almost be equivalent to time wastage.

The enforcement of fortitude and endurance by the conservatives leads to the inevitable overdilatation and, frequently, actual rupture of the pelvic floor. We who have passed through these stages of experience realize, in this attitude, the explanation of many of our still-born infants.

The "moderate" in obstetric practice might be defined as one who endeavors to obtain spontaneous labor, but combines with patience a reasonable estimate of the human capacity to work and assimilate punishment.

Fetal mortality upon this continent is stated to be at par with the highest in the world. From whence comes this scourge? Lack of education! Agreed. Perhaps it is utterly impossible to adequately reach the entire public. What of our future ambassador, the student?

Is obstetric teaching, upon the merit of its importance, in a proper position in the university curriculum? Do we, as teachers, condone or practice methods which in average hands are dangerous? To the end of time the majority of pregnant women will be under the guidance of average obstetricians.

The argument that a man may practice publicly what he dare not preach is incompatible.

The abolition of pain and fatigue will always create a great demand for service. The novice must emulate his competitor or starve.

One of these avenues is the safe road. Fetal mortality in this continent will only be reduced by honest self-investigation.

The Department of Obstetrics in McGill University professes a membership in the moderate school. Because of this we place before you the results obtained in 4,025 labor cases. May we impress upon you that these were all normal healthy women at term, about to begin or having just started in labor?

Table I gives the four blocks around which this résumé is written. The healthy or normal hospital group is virtually a report of last year's work in cases of anterior position. The healthy contracted pelvis group is a study of results in cases over the past five years. The posterior position series represents last year's experience with

this troublesome condition. The healthy group in private practice includes my own experiences of the past ten years.

TABLE I

1. Healthy Pregnant Woman Hospital Service	2. Healthy Pregnant Woman Private Practice
3. Healthy Woman with Contracted Pelvis	4. Healthy Woman with Occipitoposterior Position

TABLE II

	HEALTHY WOMAN HOSPITAL SERVICE	CONTRACTED PELVIS HOSPITAL SERVICE	OCCIPITO- POSTERIOR HOSPITAL SERVICE	HEALTHY WOMAN PRIVATE PRACTICE
Total No. Cases	2349	381	102	1193
Spontaneous Cases	1729	217	37	783
Artificial Cases	620	164	65	414
	26.8%	43%	63.7%	36.2%

Table II exhibits how these 4,025 cases were divided among the groups, with the number and percentages of artificial terminations.

An explanation of our measure of contraction might well be offered at this point. A minor degree at the brim in the diagonal conjugate means 10.5 cm., at the transverse of the outlet 8 cm.; moderate at the brim, diagonal conjugate, 10 to 9 cm., at the outlet 7 cm. Maximum diagonal conjugate 8.5 cm., or less, the outlet 6.5 cm. or less.

Table III will indicate how many of these 344 contracted pelvises were found in minor, moderate, or maximum degrees.

TABLE III

	FLAT AND FLAT RACHITIC	GENERALLY CONTRACTED	FUNNEL
Minor			
D.C. 10.5 cm.	16	15	77
Moderate			
D.C. 10 cm. 9 cm.	136	43	28
Minimum			
D.C. 8 cm. or less	44	72	8

Some definition of terms used in the succeeding pages might be of value.

Elective.—An artificial termination of labor, without specific indication of maternal or fetal distress.

Prophylactic.—When a procedure is carried out to forestall a foreseen menace.

Fetal Distress.—Measured in all of these series by changes in rate, rhythm, and volume of the fetal heart. Maternal distress recognized only in pulse changes and the quality of uterine contractions.

Table IV presents a digest of the 2,766 spontaneous cases in so far as maternal and fetal mortality was concerned. The average baby weight was 3,230 gm., average hours in labor, 15.25.

In the vast majority of primiparae, in this series, a median or lateral episiotomy was performed at the moment of the crowning of the head.

TABLE IV. SPONTANEOUS LABOR

	NO. CASES	SPONTANEOUS LABOR	MATERNAL MORTALITY	FETAL MORTALITY
Healthy hospital	2349	1729	0.11%	8 or 0.4%
Flat pelvis	196	111	0	7 or 6.3%
Generally contracted	72	56	0	1 or 1.7%
Funnel pelvis	113	50	0	3 or 6.0%
Occipitoposterior	102	37	0	1 or 2.7%
Healthy women in private practice	1193	783	0	0

There are many of us who, twenty-five years ago, spent hours in purposely delaying the perineal stage of labor. The fond hope was conservation of tissue. We have long since graduated from such teaching into a wider knowledge. The better birth conditions of our babies, the marked decrease in postpartum hemorrhage because of reserve tone in the uterine muscle, emphasize this.

The gynecologist of former days thrived upon repairs of sacrospinous hernia and prolapse. Today, from sheer necessity, he is driven into the obstetric ranks.

Of these four different types of women 2,766 or 68.4 per cent delivered themselves spontaneously, with a gross maternal mortality of less than 0.10 per cent. Strangely enough, the total maternal deaths occurred in multiparae after normal labor, two women dying of sepsis. The fetal mortality of 0.7 per cent is an extremely low one even in the confinements of healthy women. Two outstanding facts are proved, the large majority of women if left alone will, even in the face of possible dystocia, deliver themselves spontaneously of average-sized babies without great danger to themselves or to the children. We firmly believe that the performance of episiotomy, in the large majority of primiparae, may be given a great degree of credit for this low fetal wastage. To those who have never given this procedure a trial, I would recommend it to their investigation; to others who have been disappointed in their results, I would recommend a close study of their technic.

Except in two cases of prolapsed cord, all fetal deaths were due to the trauma of labor. Ten occurred in the contracted pelvis group. Possibly a more liberal view toward cesarean section might have saved them.

All fetal deaths occurred in prolonged first stage labors, more particularly in the flat pelvis.

Table V epitomizes the low forceps operation in the complete series. There will be noted a frequency of 13 per cent. The procedure in the

contracted pelvis group was totally of emergent character but productive of 50 per cent of the fetal loss in this study.

In the remaining vast majority 50 per cent were emergent; in other words emergent forceps accounted for the remaining 50 per cent of the net fetal death rate of 1.1 per cent.

There were 258 elective low forceps operations performed without one single infant loss.

It is well to note at this juncture that a child must leave the hospital alive and well to escape being counted a loss.

The average weight of these babies was 3,230 gm. The causes of death were: intracranial hemorrhage, two; intrauterine asphyxia, three; craniotomy after forceps failed in a funnel pelvis case, one.

In our clinic the use of elective low forceps after one hour's delay in the perineal part of the second stage of labor is almost universally the routine, and in primiparae is associated always with an episiotomy.

In my own private practice, as soon as internal rotation is complete, this procedure is carried out in every case at the present time.

TABLE V. LOW FORCEPS, HEALTHY HOSPITAL

	NO. CASES	LOW FORCEPS	MATERNAL MORTALITY	FETAL MORTALITY
Normal hospital group	2349	326	—	2 or 0.9%
Flat pelvis	196	5	—	0
Generally contracted	72	3	—	1 or 33.3%
Funnel pelvis	113	19	—	1 or 5.2%
Occipitoposterior	102	17	—	1 or 5.8%
Healthy private	1193	174	—	1 or 0.5%

The study of the influence of the type of woman upon the weight of her baby revealed some interesting details. The average weight of 3,147 gm. occurred in the generally contracted pelvis, the masculine funnel group exhibited an average child of 3,875 gm. The worst offender of all was the posterior position, an average of 3,910 gm. The flat pelvis, on the other hand, developed the normal average of 3,213 gm.

TABLE VI. MIDFORCEPS

	NO. CASES	MID-FORCEPS	MATERNAL MORTALITY	FETAL MORTALITY
Healthy hospital group	2349	157	0	9 or 4.9%
Flat pelvis	196	9	0	4 or 44.4%
Generally contracted	72	5	0	0
Funnel pelvis	113	11	0	2 or 18.1%
Occipitoposterior	102	43	0	5 or 11.1%
Healthy private group	1193	82	0	5 or 6.0%

Table VI presents a résumé of a very vexed question: How may we avoid the use of midforceps? It is with regret that we have to report the performance of this operation upon 307 occasions or an incidence of 7.6 per cent. To our credit it may be said, none were elective.

Midforceps is only performed in our clinic by experienced members of the staff. The average weight of babies in this group was 3,200 gm. Fetal mortality, for this group, rose to the high figure of 8.1 per cent. Studying these fetal losses, the operation seems to have been desperately fatal in flat and funnel pelvis, also in the occipitoposterior positions. It must be noted that in these funnel pelvis deaths there was an associated posterior position at the commencement of labor.

The character of the labor in these three groups, without doubt, was one of the chief factors in the end-result. Attrition produced by punishment rendered the child unable to accept further compression and anesthesia. Midforceps as an emergent operation, with us, was a dismal failure. Prophylactic midforceps was performed 36 times with a fetal death in 3 cases, a percentage of failure in over 8 per cent of cases in which this procedure was given a trial. Our attitude toward the use of this method of delivery is to place it in our judgment as an operation of last resort. Every fetus was alive at the beginning of the operation. By far the greater majority of these infant deaths was due to intracranial hemorrhage, intrauterine asphyxia being a poor second. From our own experiences we unhesitatingly condemn the use of the procedure as a universal method for the abolition of the second stage of labor.

Table VII is an epitome of high forceps extraction, until just recently, only performed as an operation of last resort and usually entering the field of activity through the door of mistaken judgment.

TABLE VII. HIGH FORCEPS

	NO. CASES	HIGH FORCEPS	MATERNAL MORTALITY	FETAL MORTALITY
Healthy hospital group	2349	15	0	6 or 40 %
Flat pelvis	196	2	0	50 %
Generally contracted	0	0	0	0
Funnel pelvis	113	2	0	1 or 50 %
Occipitoposterior	102	5	0	2 or 40 %
Healthy private group	1193	11	0	2 or 18.1%

One glance at the terrifying fetal mortality rate would seem to justify such an opinion. Under all circumstances, but one, such an attitude is absolutely sound. In all but 18 cases in Table VII, the indication was both maternal and fetal distress and for all of them we accept your criticism. Ultraconservatism again comes to the front.

We have in the past few years changed our views with regard to the posterior position. The former slogan of leaving them alone has not been found satisfactory. In all but 18 of the 65 artificial cases we have been compelled to operate under the disadvantage of acute maternal and fetal distress. Last year there was an incidence of 102 such cases, primiparae 50, multiparae 52, including R.O.P. 67, L.O.P. 35. Of the L.O.P. cases 28 required a terminal operation, in R.O.P., 32 needed assistance. Spontaneous labor resulted in one fetal death, 2.7

per cent; artificial labor in eight or 12.3 per cent. In these deliveries all deaths were due to trauma.

For years we have recognized two types of posterior position, one starting labor with the membranes ruptured, in the other the membranes remaining intact until the cervix is fully dilated.

In dealing with these conditions we hope to escape the charge of encouraging the abolitionist. The situation is a very grave one, extremely costly in fetal wastage, no matter how dealt with, except by selective cesarean section. The price paid by the young bride in the cesarean section column is of course appreciated.

In the dry labor group we have waited until the lower uterine section has been thinned out completely, leaving only the paper-like edge of the os. With membranes intact, labor is allowed to proceed until the cervix and os are no longer factors. In the former, under deep anesthesia, the cervix is manually dilated or incised. In both, the head is pushed deliberately out of the pelvis, Pomeroy's maneuver performed, forceps applied, and the head brought down in the opposite anterior position with Barton, Kielland or other forceps according to the predilection of the operator. In using the Pomeroy maneuver we have been, upon occasion, embarrassed by prolapse of the cord. Dr. G. C. Melhado of this clinic has perfected a simpler and, in our experience, a much easier maneuver. The head is pushed out of the pelvis, and grasped with the palm of the hand over the posterior ear; it is then rotated to the transverse diameter of the pelvis; the posterior forceps blade is passed between the palm of the hand and the posterior ear; the anterior blade is simply rotated around the face to lock with its mate. Further rotation of the occiput to the anterior quadrant of the same side has proved an easy matter in all cases. The ease with which the head descends is really most amazing. In the 10 cases in which this simple technic was applied no grave maternal damage occurred and every child was born alive. We commend it to your investigation. In acting thus in anticipation of impaction we have delivered in all 18 women, 10 primiparae and 8 multiparae without fetal loss.

We point somewhat with pride to our breech results, shown in Table VIII; possibly we are not too heavily inflicted with them. The average weight of these babies was 3,393 gm. The insistence of non-interference in every case of breech until the body of the fetus up to

TABLE VIII. BREECH

	NO. CASES	BREECH	MATERNAL MORTALITY	FETAL MORTALITY
Healthy hospital group	2349	76	0	5 or 6.5%
Flat pelvis	-	-	-	-
Generally contracted	-	-	-	-
Occipitoposterior	-	-	-	-
Healthy private group	1193	38	-	1 or 2.6%

the level of the umbilicus was completely born, has been one of the main reasons for a gross mortality in a total of 114 births of but 5.2 per cent, as compared with a general average of over 10 per cent. Lately we have begun the application of forceps upon the aftercoming head as recommended by Piper of Philadelphia, and from our experience of this technic so far we expect to make a further reduction in our losses.

Every fetal death in this series was due either to cerebral damage or a broken neck. It may be fitting here to speak of a teaching fault, namely, the old direction to wait only so many minutes after the umbilicus appears, the vigor, resultant of this time limit to my mind, has produced more fatalities of the newborn than any other step in the technic. Personally we overemphasize the necessity of taking all the time needed; personally I have found it very hard indeed to use up five minutes.

The assurance of making the anterior arm come down in front of the head by Potter's maneuver with pressure downward and backward upon the inferior angle of the scapula has helped a great deal indeed.

Version and extraction in the Royal Victoria Maternity Hospital is almost totally an operation of emergency. The very fact that in a series of 4,205 (Table IX) confinements, version and extraction have been performed only upon 42 occasions, and of these but 5 were elective, indicates clearly the affection and faith in which we hold it. Fetal mortality in elective cases was 20 per cent, in the emergent, 37.8 per cent. The indications in the emergent class were uniformly positive, face and transverse presentation, prolapsed member, prolapsed cord.

TABLE IX. VERSION AND EXTRACTION

	NO. CASES	VERSION AND EXTRACTION	MATERNAL MORTALITY	FETAL MORTALITY
Healthy hospital	2349	16	0	8 or 50 %
Flat pelvis	196	7	0	6 or 87 %
Generally contracted	0	0	0	-
Funnel pelvis	113	2	0	0
Occipitoposterior	0	0	0	0
Healthy private	1193	17	0	1 or 5.8%

The desperate chances of the baby in the flat pelvis group is most vividly shown. In these cases the condition of the fetus at the commencement of operations was in all cases better than fair. One hears the justifiable criticism, "Not doing this often enough, small wonder you fail." We heartily agree. Is it not then a very just reason for a generous condemnation of this modern attempt to popularize a procedure which, even in an institution especially equipped and under the care of fairly well trained and experienced obstetricians, is so eminently destructive?

Always if possible in our clinic an elective operation, performed in this series, 141 times, of which 4 were emergent cases (Table X). The gross fetal mortality among these 141 babies was 2.8 per cent. Three died before leaving the hospital, one from hemorrhagic disease, a second from inanition, the third from congenital occlusion of both ureters. Two died within forty-eight hours of delivery, both from the trauma of labor, which was well advanced before admission to the hospital.

TABLE X. CESAREAN SECTION

	NO. CASES	CESAREAN SECTION	MATERNAL MORTALITY	FETAL MORTALITY
Healthy hospital	2349	27	0	2 or 14 %
Flat pelvis	196	41	0	1 or 2.5%
Generally contracted	72	4	0	0
Funnel pelvis	113	18	0	1 or 5.5%
Healthy private	1193	88	0	0
Occipitoposterior	102	0	-	-

The low cervical, extraperitoneal and classical operations are used; the majority of patients, however, were operated upon by the classical technic.

We freely admit an ultraconservatism in our attitude toward this surgical procedure. The indications in our clinic must be almost positive, especially in the contracted pelvis group, and the majority of our cesarean operations was performed in this class. In a young woman under thirty, unless the disproportion was definite, or a history of previous attempt with failure was obtained, the patient was subjected to the definite trial of labor. Labor once thoroughly established, we considered the door to section closed. Many of our mid- and high forceps operations and three of our craniotomies were the reward for this stand. Mistakes of bad judgment, yes, but in good conscience.

The safety of the extraperitoneal operation has never deeply impressed us.

TABLE XI. DESTRUCTIVE OPERATIONS

	NO. CASES	DESTRUCTIVE OPERATION	MATERNAL MORTALITY	FETAL MORTALITY
Healthy hospital	2349	1	0	1 or .05%
Flat pelvis	196	4	0	4 or 2.04%
Generally contracted pelvis	72	0	0	0
Funnel pelvis	113	1	0	1 or .8%
Healthy private	0	0	0	0
Occipitoposterior	0	0	0	0

The one evidence I can offer in rebuttal in these 141 cesarean sections is the consistent zero mark in the column for maternal mortality. In fact, may we draw your attention to the maternal mortality column, in all procedures developing in the care of these 4,025 women, to the almost negative death rate.

Table XI is a study of these regrettable end-results and will expose the guilt of the flat pelvis. Three of these patients were brought to the hospital in such condition that other procedures were impossible. Two of the babies were already dead. The almost universal escape of the generally contracted pelvis from the complication of labor or as a great factor in fetal mortality is interesting and instructive.

Table XII demonstrates the frequency of the different types of labor in percentages. Opposed is a corresponding estimate of how much fetal loss each added to make up the whole. The three great offenders stand out all too prominently, mid- and high forceps, version and extraction, the greatest criminal of the three being version and extraction.

TABLE XII. GROSS FETAL MORTALITY 2.3 PER CENT IN 4205 CASES

	SPONTANEOUS DELIVERY USE	LOW FORCEPS USE	MIDFORCEPS USE	HIGH FORCEPS USE	BREECH DE- LIVERY USE	VERSION AND EXTRACTION USE	CESAREAN SECTION USE	DESTRUCTIVE OPERATION USE
Frequency	PER CENT 68.4	PER CENT 16	PER CENT 7.6	PER CENT 0.84	PER CENT 2.8	PER CENT 1.4	PER CENT 0.34	PER CENT 0.14
Fetal mortality	0.47	0.14	0.62	0.29	0.14	0.3	0.9	0.14
Maternal mortality	0.4	-	-	-	-	-	-	-

TABLE XIII. CAUSES OF FETAL DEATH

Intracranial hemorrhage	37	} 55-----59.1%
Intrauterine asphyxia	12	
Craniotomy	6	
Other	38	-----40.9%

Table XIII is a diagram of the causes of fetal death. A glance is all that is necessary to make us realize the futility of interference as a means for conservation.

CONCLUSIONS

1. Episiotomy is one of the best procedures of a moderate school.
2. Elective low forceps is a very close second.
3. The pelvic floor and perineum are in the vast majority of cases conserved by the combination of these two.
4. Emergent or prophylactic low forceps is the best way out of a bad hole.
5. Breech extraction, under modern improved technic, need not become the cause of so much fetal loss as in the past.
6. The occipitoposterior position still demands our deepest respect, but does not compel the same old fear.

7. Cesarean section is not 100 per cent safe for the child, because, of the intrauterine fetus we really know nothing.

8. It is not consistent with good judgment to interfere with the normal healthy woman, unembarrassed by complication of pelvis or position, who, if left to herself, will in 71 per cent of cases deliver herself without maternal or infantile injury.

9. Conversely, it savors almost of the insane to introduce, as agents for the relief of pain, fatigue and a much exaggerated amount of tissue damage, operative procedures responsible for 80 per cent of the fetal mortality exhibited here.

10. The "radical" of obstetrics, in our humble opinion, is to be found at either end of the chain, in the conservative and abolitionist camp.

11. For the former we believe there is hope. Surgery seems to be the only treatment for the latter.

In the opening of my address to you I used a quotation from Professor W. W. Chipman; in closing may I use another of his, "If it is important to be in the world at all, and most of us act as if it were, the manner and safety of our entrance are surely a first consideration."

We would like to express our gratitude to Dr. Leon McGoogan of Green Falls, Mass., for the use of the figures derived from his splendid study of our contracted pelvis cases.

MEDICAL ARTS BUILDING.

Terrades: A Case of Ovarian Tumor Recurring After 16 Years. Rev. espan. de obst. y gynec. 15: 121, 1929.

The patient, forty-six years old, single, had a tumor of the right ovary, weighing 7 kg. removed in 1912. The tumor is described as having been epithelial and composed of cystic cavities. Before operation she had amenorrhea, change of voice, and hypertrichosis for three years, all of which disappeared after it.

Sixteen years later (1928) she was again admitted with a large fluctuating abdominal mass, some ascites, and amenorrhea for ten months. At operation the same kind of tumor, weighing 6 kg., attached to the omentum by large vessels and also to the intestines, was found. The pedicle was attached to the abdominal wall, 4 cm. below the umbilicus. There was no connection between tumor and pelvic organs. The postoperative course was normal and the patient immediately regained her menstruation.

The author believes that the recurrence was due to implantation following the first operation, resulting in a slow growing tumor which attached itself to the omentum, and received its nutrition from it. The amenorrhea was due to an inhibition and neutralization of the ovarian hormone by the secretion elaborated by the tumor cells.

FRANK SPIELMAN.

THE SURGICAL PATHOLOGY OF THE FIBRINOPLASTIC OR ADHESIVE VARIETY OF TUBERCULOUS PERITONITIS

By J. W. KENNEDY, M.D., PHILADELPHIA, PA.

UPON several occasions within the recent past I have heard prominent teachers tell medical students that the adhesive variety of tuberculous peritonitis was unsurgical and that good surgical results could be expected only with the miliary and ascitic varieties of tuberculous peritonitis.

This, I feel, is a very grave mistake and should not be transmitted to our student body as surgical teaching.

The opinion that the patient with an adhesive variety of tuberculous peritonitis is doomed to a short life is a statement which I have seen refuted a great number of times.

The immediate urge of the writing of this paper is an interview this morning with a patient who was operated upon for the fibrinoplastic variety of tuberculous peritonitis in the Joseph Price Hospital over a quarter of a century ago. This patient was in a perfect state of health, showing no evidence of tuberculous trouble, although she had been operated upon for the adhesive variety of tuberculous peritonitis in which the entire intestinal canal was found in a conglomerate mass resembling a solid tumor.

We have found a large number of patients living from five to thirty years who underwent a similar operation for the same tuberculous condition.

It is with a feeling of regret and apprehension that I view this teaching, namely, that the condition of fibrinoplastic variety of tuberculous peritonitis is unsurgical. On the contrary I know of no condition in the abdominal cavity where thorough surgery is more rewarded.

Many times I have seen a mere skeleton of a patient return to full weight, resume her former occupation and also excel in athletic sports and exhibit feats of strength and endurance.

Certainly in 95 per cent of the patients who have come to the Joseph Price Hospital during my thirty years' association with the institution, we have been able to separate all of the adhesions existing between the coils of the intestine and adjacent viscera, and nothing short of this thorough surgery will be rewarded by a great percentage of successes. The tuberculous peritoneum will stand surgical manipulation with less degree of surgical shock than the normal peritoneum and so will any peritonitic peritoneum. This principle we have discussed a number of times elsewhere.

We do not consider any incipient or chronic tuberculous lesion of the lungs or kidney a contraindication to thorough surgery for tuberculous peritonitis; we are concerned with the question of tuberculous dosage.

I have seen incipient tuberculous lesions of the lungs clear up following thorough surgery for the adhesive variety of tuberculous peritonitis; just as we have seen an incipient tuberculous lesion of the kidney remain symptomless after removal of the other kidney for an advanced tuberculous lesion.

We have also seen this principle exemplified in the removal of large malignant ovarian cysts which were the parents of numerous infant daughter cysts which were scattered throughout the abdominal cavity, the numerous small cysts disappearing after removal of the extensive parent growth and the return of the health and resisting powers of the patient.

In operating on the patient with the adhesive variety of tuberculous peritonitis we proceed as follows: If there is any portion of the bowel free from adhesions or any line of cleavage leading into the tuberculous mass, we start at this point and break all adhesions between the coils of intestines, exposing both sides of the mesentery, which simply means that the ultimate adhesions must be broken. The adhesions must be broken by expression or pressure by the thumb and fingers, the force being used at the expense of the adhesions and not the bowel wall—this is most important.

All tuberculous structures which permit amputation should be removed, such as the appendix, tubes and ovaries and as much of the involved omentum as possible, in order to assist in reducing the dose of the tuberculous lesion.

In my opinion the tuberculous infection is continued from the absorption that takes place between the adherent surfaces, and it is here that later necrosis and caseous degeneration take place. Furthermore, the breaking of all adhesions helps to release partial chronic bowel obstructions, the stasis of which must cause a harmful degree of infection from the mucous membrane of the enteron and thus help lower the natural resistance of the patient.

During the operation as the adhesions are broken and surfaces exposed, they are dusted thoroughly with iodoform. It is astonishing the amount of iodoform these patients can stand. Evidently the power of absorption of the tuberculous peritoneum is reduced to a minimum, yet these patients will have a metallic odor to their breath for several days after operation apparently with no harmful result.

The advantages of the radical surgery by which all adherent tuberculous surfaces are separated, are clearly indicated by those patients who had undergone an abdominal operation which consisted of merely opening the abdomen and was abandoned when the adhesive variety

of tuberculous peritonitis was discovered. When these same patients later were operated upon in the Joseph Price Hospital by the method indicated in this paper, brilliant results were obtained.

We do not drain these patients. Every possible care should be taken to prevent a postoperative fistula. Tuberculous fistulas are not prone to close spontaneously.

I have often been asked about the effect of the iodoform. I am not sure whether the beneficial effect is due to its bactericidal power or whether the irritation from the iodoform causes a helpful hyperemia.

The very radical surgery which is incident to breaking all the adhesions and exposing all possible tuberculous surfaces, certainly causes a marked operative hyperemia, and this may be one of the most important factors in recovery.

It is my opinion that the iodoform does help to prevent return of the adhesions and may do so by retarding early bacterial invasion.

Dr. Price called attention to two patients upon whom he had operated several years before for the adhesive variety of tuberculous peritonitis; he did not have sufficient iodoform at the time of the first operation to cover the peritoneal surfaces after separating the adhesions. He operated on these same patients later and found those areas that he had not dusted with iodoform firmly adherent, whereas the other surfaces which had been properly treated with iodoform were quite free from adhesions.

If the tuberculous patient comes to surgery at that late stage which may be called caseous, which means degeneration has already taken place, this will probably prevent the radical surgery which I have already indicated, as the visceral structures will be necrosed and will not stand manipulation.

I have seen the omentum nearly two inches thick and so very brittle that it would break upon manipulation, and yet even these late cases must be given a chance.

I feel that the surgical pathology of peritonitis in general will have to be rewritten. The "sacred" adhesion must not prevail.

Better surgery must be taught and done in the peritonitic abdomen, and the patient with the adhesive variety of tuberculous peritonitis should be placed on the surgical list and will often give the most brilliant results when in an apparently hopeless condition.

241 NORTH EIGHTEENTH STREET.

VESICOABDOMINAL FISTULA AS A COMPLICATION OF LABOR

BY HONORIA ACOSTA-SISON, M.D., MANILA, P. I.

(From the Departments of Obstetrics and Gynecology, University of the Philippines)

FISTULA involving the bladder wall in cases of prolonged obstructed labor is not unusual. It is one of the complications to be feared by the obstetrician after a difficult forceps extraction or after a prolonged impaction of the head within the pelvic cavity. Vesicoabdominal fistula (or one which communicates the bladder with the abdominal wall or peritoneal cavity) as a complication of labor, however, is one that has not been described in the obstetric and gynecologic textbooks, monographs or journals to which I have access. As far back as 1885, only a few cases of vesicoabdominal fistula have been reported, but they occurred as complications of abdominal operations (Whiteside), abscess (Buckingham), vesical tumors (Whiteside), or accidents from x-ray burn (Ottow). There was one vesicointestinal case (Marcey) that resulted after an unusually strenuous exercise.

In the Philippine General Hospital from the date of its establishment in 1910 to December, 1929, there have been 41 cases of vesical fistula, 37 of which were vesicovaginal, as follows:

After prolonged labor ending in forceps delivery	14
“ “ “ “ “ podalic version	6
“ “ “ “ “ embryotomy	1
“ “ “ “ “ spontaneous delivery	11
“ stone removal per vaginam	2
Cause not stated in history	3

In one of these three cases, the fistula was vesicovaginorectal. Five cases, four male and one female, were diagnosed as vesicoabdominal fistulas and were all complications of abdominal operations, two of them being for suprapubic removal of stone from the bladder. As in all of them the urine made its exit through the abdominal wound, diagnosis was easy.

The barrenness of medical literature concerning vesicoabdominal fistula as a labor complication and the importance of its recognition, especially when the urine is retained within the abdominal cavity, prompted the author to report the following two cases:

CASE 1.—S. P., primipara, twenty-one years of age, was admitted to the obstetric ward on July 30, 1929, with the complaint of labor pains. On admission she was anemic and asthenic. For a month before admission, she had been having an irregular low fever and frequent micturition. The bag had ruptured prematurely

and the head which was in R. O. P. position was impacted on the perineum with no progress in spite of two hours of strong expulsive pains. A low forceps application was made and a live small baby weighing 2200 gm. was extracted by Dr. Barican. In the afternoon and evening after the operation, she complained of much abdominal pain and inability to urinate. She was catheterized but only 5 c.c. of urine were obtained. On the second day, she vomited ascaris twice and complained of epigastric pain, hunger, and anorexia. On the third day, she moaned on account of epigastric pain and painful defecation. On the fourth day, she vomited yellowish material, and on the sixth day, a pear-shaped cystic tumefaction in the bladder region was noticed. Vaginal examination showed bulging of the anterior fornix and the cervix uteri was high. Catheterization obtained only 200 c.c. of bloody urine. Ever since the delivery the patient had a low septic temperature ranging from 37° to 38.5° C. The pulse, however, was rapid, from 120 to 140. The uranalysis made on August 18, or tenth day of puerperium, was as follows:

Pale, thick and foul; albumin heavy; abundant erythrocytes and pus cells; many finely granular casts and a few squamous and epithelial cells. Stool examination



Fig. 1.—Diagrammatic view of the false urinary sac in Case 1. It is connected with the shrunken bladder by an opening at the upper portion.

showed abundant ascaris eggs. Blood culture negative. Leucocyte count gave 19,000; neutrophils, 70; small lymphocytes, 20; large lymphocytes, 4; large mononuclears, 3; eosinophiles, 3.

The bladder was irrigated daily with borax solution and grayish necrotic particles came out with the irrigating fluid. Apparently all the solution introduced, which was not more than 20 c.c. at each instillation, was always recovered. The cystic painless pear-shaped tumefaction over the bladder region kept increasing slowly in size. Throughout, she urinated spontaneously but in small amounts. She progressively became weaker and died on the twenty-eighth day of the puerperium. On autopsy the pathologist, Dr. Barrera gave the following report: Chronic localized peritonitis, gangrenous cystitis with perforation of the anterior wall and formation of a large inflammatory sac of pus and debris, chronic purulent endometritis and endocervicitis, and parenchymatous degeneration of all visceral organs. Occupying the normal place of the bladder was a purulent necrotic sac bounded anteriorly and laterally by the abdominal wall and superiorly by a thick layer of fibrinous exudate which matted together the loops of the small intestine. The sac was

connected below by an opening the size of a finger tip on the anterior wall of the bladder which had shrunk to a small cavity the size of a chicken's egg toward its fundus. (Fig. 1.)

CASE 2.—B. A., twenty-three years of age, primipara was admitted to the Hospital on October 7, 1929, with the complaint of prolonged strong labor pains and impaction of the fetal head in the pelvic cavity for twelve hours before admission. The lower extremities were markedly edematous for three weeks before admission. The external genitalia also became edematous after the onset of labor. Patient was prepared for forceps delivery under chloroform anesthesia but she delivered spontaneously a stillborn full-term fetus before the instrument could be introduced. There was no perineal laceration but the vagina was widely gaping. Six hours after delivery, patient had two convulsive attacks followed by unconsciousness. She became conscious a few hours after the second convulsion but throughout the puerperium she was weak and dull. The temperature since the first day was irregular and septic in character ranging from 37.5° to 40.5° C. The bladder was atonic so that it had to be emptied by catheterization and at times as much as 1 to 1½ liters of urine were obtained. The uranalysis made on the twelfth day when she died showed a thick turbid urine with heavy albumin, granular casts, and abundant erythrocytes and pus cells. The leucocyte count was 27,800; polymorphonuclear 96 per cent; small lymphocytes 4 per cent. The autopsy findings by the aforementioned pathologist were: Acute serofibrinous peritonitis, gangrenous cystitis with incomplete perforation of the bladder on the anterior wall, pyelonephritis, acute endometritis, congestion of the brain and parenchymatous degeneration of all the organs. The bladder was filled with thick opaque urine. The mucosa specially at the posteroinferior part was thickened and markedly gangrenous. At the upper part of the anterior wall or at the apex was a small necrotic area the center of which was perforated as far as, but not through the serosa. The serous covering was however so thin and weakened that on stretching the bladder it was easily torn through. Much serofibrinous exudate was found in the neighborhood of this perforation.

DISCUSSION

The interest in these cases is the apparently unusual location of the perforation on the anterior wall of the bladder near the apex which the author believes to be *locus minoris resistentiae* on account of its nearness to the symphysis. The location is such that an incomplete perforation, as in Case 2, must often escape notice unless cystoscopy is made. Perhaps if carefully searched for, it will be found more frequently in those cases of labor where the head remained impacted within the pelvic cavity for a long period, followed by urinary disturbances during puerperium and supposed to have died of pelvic inflammation. Both of the patients were primiparas. Primiparas would seem to be specially predisposed on account of the tendency of the head to engage during the last months of pregnancy, pressing on the bladder, and favoring a cystitis which weakens the resistance of the bladder wall, especially in patients who are anemic and asthenic as in Case 1. The patient in Case 2 was also weak on account of nephritic toxemia. Both had prolonged impaction of the fetal head within the pelvic cavity. The one that had impaction of longer duration delivered

spontaneously a stillborn child, while the other that was relieved by a low forceps extraction had a live child. In both the cause of the perforation was undoubtedly the prolonged pressure on the bladder wall which was sandwiched between the hard symphysis and the fetal head.

That pressure necrosis alone and not forceps application was the cause in Case 1 was shown by the absence of injury on the vaginal wall, or of a vesicovaginal fistula which would have resulted if the instrument was the causative agent. The perforation was larger than in Case 1, the urine passed through the bladder wall and had dissected its way between the peritoneum and lower abdominal wall, and a thick inflammatory sac had formed in front of the uterus where the bladder should be. That pressure necrosis was also the true cause in Case 2 was shown by the fact that the gangrenous changes were most marked at the lower posterior wall on account of the stagnation of the urine in that locality, the perforation took place at the upper part of the anterior wall nearest the symphysis pubis. The perforation was not complete and it developed slowly. The serous coat of the bladder was apparently intact enough to keep the urine within the bladder. From the autopsy findings, however, it could be seen that it was only a question of time before the serous wall would have given way.

As to the possibility of diagnosing the condition: Since the perforation in Case 2 was incomplete and the urine had not leaked beyond the bladder wall, the perforation could not have been suspected *in vivo*. The failure of diagnosing the true condition early in Case 1 was due to the fact that the pear-shaped enlargement was at first mistaken for the subinvolted infected uterus. The pelvic pains were attributed to uterine infection and the epigastric pains and vomiting which must have been caused by the local peritonitis, were assumed to be due to the ascariasis. The bloody urine was attributed to acute cystitis. The fact that the patient urinated spontaneously and that fluid introduced into the bladder was recovered made us doubtful as to the presence of a vesicoabdominal fistula which was supposed to be necessarily accompanied by extravasation of urine into the peritoneal cavity. However, the cystic character of the enlargement, its increase in size coincident with scanty micturition, the abnormally high location of the cervix, and the cystic bulging of the anterior fornix not diminished by catheterization were unmistakable signs of encapsulated urine outside the bladder. The only condition it could simulate would be an ovarian cyst or an ectopic pregnancy. But the history of the development of the enlargement, the absence of scanty micturition and the characteristic finding of an exploratory puncture of the tumor would eliminate the former. Cystoscopy would probably establish the diagnosis.

TREATMENT

The prophylactic treatment would be to watch the progress of the presenting part carefully during the second stage specially in those cases with premature rupture of the bag. If in the presence of strong expulsive pains recurring at frequent intervals no progress is observed in one or two hours, it is a conservative measure to extract the child according to the method suited for each case always with due consideration for the integrity of the maternal soft parts. The bladder should be emptied before each operation. The manner of passing urine, its character and amount should be carefully noted in the first days of puerperium to eliminate the possibility of vesical fistula. This is especially true in operative labors. And in cases of bladder paresis where all the means of inducing spontaneous micturition fail, aseptic catheterization at regular intervals should be made. In these cases, the bladder should not be allowed to retain more than 300 or 400 c.c. of urine at any one time.

As for the curative treatment, in a small fistula like the one observed in Case 2 a retention catheter and a judicious irrigation of the bladder with small quantities of mild aseptic solution may inaugurate spontaneous healing. But when the urine has passed beyond the limit of the bladder wall, the obvious treatment would be abdominal drainage of the urinary sac, the use of the retention catheter and repair of the perforation as soon as the tissues normalize.

SUMMARY

1. Injury to the bladder wall which may result into a vesicoabdominal fistula is a complication that must be guarded against in all cases of prolonged dry labor with impaction of head in the pelvic cavity and accompanied by strong ineffectual expulsive pains.

2. Vesicoabdominal fistula is not necessarily accompanied by extravasation of urine into the abdominal cavity for the peritoneal covering may resist, in which case the urine dissects its way beneath the loose subperitoneal tissue and becomes encapsulated.

3. Scanty urination, especially if bloody, and the presence of a recent, rapidly increasing cystic enlargement corresponding to the bladder region which persists after catheterization, and the high location of the cervix, are characteristic signs of a vesicoabdominal fistula with encapsulated urine. Cystoscopy may definitely establish the diagnosis. Ovarian cyst and ectopic pregnancy are conditions which may remotely simulate it.

4. Timely and appropriate intervention in cases where labor test has failed and prompt attention given to cystitis during pregnancy are measures to be observed. The rational curative treatment should be abdominal drainage of the urinary sac, the introduction of a urethral retention catheter and the repair of the perforation via the abdominal route.

REFERENCES

- (1) *Whiteside*: Northwest Med. 15: 1916. (2) *Buckingham, C. E.*: Boston Med. J., 1885. (3) *Ottow, E.*: Zentralbl. f. Gynäk., 1927, No. 46. (4) *Marcey, H. O.*: Ann. Surg. 29: 1899. (5) *Schmitz, E. F.*: Surgical Clinics of North America, October, 1925.

1002 TAFT AVENUE.

WALTER CHANNING AND ETHERIZATION IN CHILDBIRTH

By HERBERT THOMS, M.D., NEW HAVEN, CONN.

THE introduction of anesthesia and anesthetic methods into obstetrics in civilized countries was accomplished only after opposition which was characterized by unintelligence, bigotry, and religious intolerance. In our own country even today, one still sees occasional evidence on the part of the laity of opposition to the use of such benignant therapy, the dying echoes of a once raging conflict.

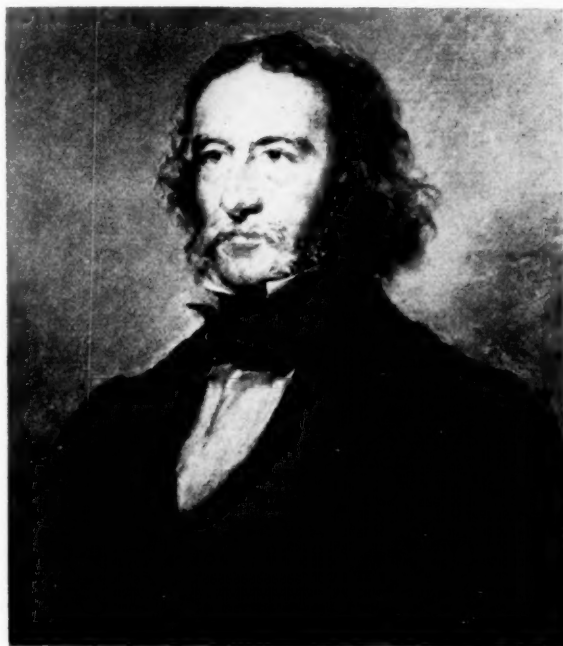
Associated with the early days of this long and important struggle appear two men whose names will not be forgotten by those who share the benefits of their endeavor. These are Sir James Y. Simpson of Edinburgh and Walter Channing of Boston. The story of the former is well known, and has been many times recorded, while that of our own countryman may be somewhat unfamiliar to the readers of this publication.

Walter Channing interests us not alone because of his important rôle in the introduction of anesthesia in obstetrics but also because he was one of America's eminent obstetric teachers, and among other achievements was the first to describe a clinical entity which will alone immortalize his name as long as anemic states of the blood are studied.

Walter Channing was born in Newport, Rhode Island, April 15, 1786. His father, an attorney, was at one time Attorney General of the State, and his mother was Lucy Ellery, daughter of William Ellery, a "Signer" of the famous Declaration. He was one of three brothers, all of whom had illustrious careers. The fame of his elder brother, the Rev. William Ellery Channing, is too widespread to need more than mention, while his younger brother, Edward T. Channing, was remembered by many generations of Cambridge students as the Professor of Rhetoric from 1819 to 1851 in Harvard University. Walter and Edward Channing entered Harvard together in 1804, in the class with their cousin, Richard H. Dana, the poet. Because of participation in his junior year in the well-known students' rebellion, Walter Channing left college, and thus failed to secure his bachelor's degree in regular course, although it was bestowed upon him later. He immediately entered into the study of medicine, and pursued his studies in Boston, Philadelphia, Edinburgh, and London. In 1809 he received his M.D. from the University of Pennsylvania, and Harvard conferred upon him

the same degree *ad eundem* in 1812, shortly after his return from his studies in Europe. In May, 1815, he was elected Lecturer in Midwifery, entering the medical faculty with Jacob Bigelow and John C. Warren, the latter succeeding his father as Professor of Anatomy and Surgery. Three years later Channing was given a full professorship in Obstetrics and Medical Jurisprudence, a position which he held until 1854.

At the first regular organization of a medical faculty connected with Harvard which took place in Boston November 1, 1816, Channing, who had been secretary of the professors of the school, was elected dean,



DR. WALTER CHANNING

Portrait by Ames

(Courtesy of Mr. Walter Channing, Boston, Mass.)

the office having been created at that meeting. On October 6, 1818, we find a vote recorded by the corporation that "the lecturers in *Materia Medica* and Botany, and Midwifery be denominated Professor in their respective departments, having rights and duties according to the Statutes of the Medical Institution of the University, but without any claim to compensation other than the fees they may receive from their pupils." A circular in 1823 states, "Midwifery and Medical Jurisprudence, Dr. Channing Fee \$10," and as early as 1827 a course of lectures in Midwifery was advertised by Walter Channing, to be given in the summer months.

In his private practice he was chiefly interested in obstetrics, and he was one of the first attending physicians at the Boston Lying-In Hospital. He was also for many years on the visiting staff of the Massachusetts General Hospital. He was one time librarian of the Massachusetts Medical Society, and an Honorary Fellow of the Obstetrical Society of London.

Shortly after ether was introduced at the Massachusetts General Hospital, Walter Channing became interested in its application to childbirth, and it was through his influence more than any other that its use became known in this country.

It is difficult for us in this day to realize the great opposition that came into being largely as a result of the efforts of Simpson and Channing to introduce anesthesia in childbirth. Not only the laity and the clergy but many members of the medical profession were unyielding in their attitude toward this innovation. These medical opponents were the most powerful in their denunciation. In the process of parturition they maintained that pain was "a desirable, salutary, and conservative manifestation of life force." The religious objections urged by the clergy were based chiefly upon the primeval curse upon womanhood found in Genesis 3:16, which reads in part, "Unto the woman he said . . . in sorrow thou shalt bring forth children."

Channing's important contribution was entitled, *A Treatise on Etherization in Childbirth*, and was published in Boston in 1848. It was dedicated to James Jackson, Professor Emeritus of Theory and Practice of Physic at Harvard. In the beginning of the volume the author says, "Occupying a somewhat public position as a teacher of Midwifery, a department of Medicine which has derived special and vast benefit from the discovery referred to, it seemed not out of place for me to collect and present to the profession, the results of its application, among ourselves and elsewhere, to that branch of the medical art." In speaking of the plan and object of the work, Channing tells us of the condition existing at the time of its publication. "Etherization was in use here, and in different parts of the country, in midwifery practice. We were hearing of results through journals and newspapers. They existed alone. The thought occurred to me that, with very little personal trouble, I might collect from various sources, facts in regard to etherization which would, in a much surer manner, make my work useful, than would anything of my own which it might contain."

Another item of historical interest has come down to us in a letter written to Sir James Simpson by Professor Charles D. Meigs, who was professor of Obstetrics at Jefferson Medical College. Perhaps it might be expected that the man who opposed so strongly Oliver Wendell Holmes's contention of the contagiousness of puerperal fever would

also be reactionary with regard to anesthesia in midwifery. However, it is undoubtedly true that Meigs voiced not only his own but the opinion of many obstetric leaders of his day when he answered Simpson's query as to the status of anesthesia in midwifery in America. In characteristic style Meigs replied, "As to its employment here (in Philadelphia) . . . I think it has not yet begun to find favor with accoucheurs. I have not exhibited it in any case; nor do I at present know of any intention in that way entertained by the leading practitioners of obstetric medicine and surgery, in this city. . . . But should I exhibit the remedy for pain to a thousand patients in labor, merely to prevent physiologic pain, and for no other motive, and if I should in consequence destroy only one of them I should feel disposed to clothe me in sackcloth and cast ashes on my head for the remainder of my days. What sufficient motive have I to risk the life or death of one in a thousand, in a *questionable attempt to abrogate one of the general conditions of man?*" What a difference in viewpoint is that of Channing, who says of his book, "It treats of a noble subject—the remedy of pain."

Before the publication of his treatise, Channing had circularized many physicians so that he was able to present in addition to his argument the results of anesthesia in 581 cases of childbirth. With this material he presented adequate proof of its beneficence and safety. The religious objections, however, were not to be met with clinical data. The same opposition that Simpson faced abroad was equally determined in America. Channing's essential argument in meeting these opponents was that the application of agents of nature to the relief of pain was also the use of God-given means by God-given powers. The situation was not wholly devoid of humor, and in discussing this phase of his subject Channing could not resist the following: "The interest in our subject," he writes, "has extended beyond the medical profession, and has even reached the pulpit. A sermon was preached here a few weeks since, on the introduction of etherization, and excited some interest. The text was, 'Deliver us from Evil.' Said one to a friend, as he left the church, 'How did you like our sermon?' 'Very well,' was the reply. 'It is not wholly wrong to lessen or destroy pain. We may eat peppermints!'"

It is interesting to note that Channing's old teacher, Benjamin Rush, had believed that "pain does not accompany childbearing as an immutable decree of Heaven," and again, "I have expressed hope . . . that a medicine would be discovered that should suspend sensibility altogether, and leave irritability or the powers of motion, unimpaired, and thereby destroy labor pains altogether." And so Channing's book stands out today not only as a scientific accomplishment but as an historical document. One cannot scan its pages without feeling the

honesty and earnestness of purpose of the author. Sir James Simpson found a worthy compatriot in Walter Channing who more than anyone else won the fight of anesthesia for America.

It is interesting for obstetricians to know that Channing is great not only as a champion of anesthesia but also because of his reputation as a teacher of Obstetrics at Harvard. He was an author of considerable note. He wrote a volume of poems, and his *Physician's Vacation*, published in 1856, gives us not only a fine record of European travel but a splendid portrayal of Sir James Simpson, at whose home Channing stayed while in Edinburgh. Among his medical publications perhaps the greatest interest is found in his *Notes on Anhaemia principally in its connection with the Puerperal State, and with Functional Disease of the Uterus; with cases*, published in 1842. This is the first recorded description of so-called hemolytic anemia of pregnancy. There is one paragraph from this excellent contribution which gives remarkable insight into the extraordinary mind of its author. In speaking of the treatment of the condition he writes with almost prophetic vision, "The question of Transfusion has often occurred to me. But of what possible benefit would be such a supply of blood? What might not the effect be of filling almost empty vessels with a fluid so unlike that which already circulates in them, and which their own functions have produced? In a disease so fatal, some risk might be incurred. But is Transfusion an operation which our present knowledge of it would authorize? If safe in itself, however, *might not time be gained by the operation, for such functional changes to occur as would supply healthful blood?*" (Italic matter is the author's.)

Walter Channing is described as of medium height, florid complexion, with blue-gray eyes. He was devoted to his family and brought up five grandchildren. He was a great admirer of his brother William, and is said to have inaugurated a joke which had a considerable circulation. Some one calling at the doctor's house asked for Dr. Channing. His reply was, "Which Doctor Channing? My brother preaches and I practice." The ever-present fun in his make-up also cropped out in his lecture room. One summer afternoon, when after fruitless efforts to talk down an organ grinder, he remarked as he took his seat, "Apollo, gentlemen, was the god of music as well as of physie." As a lecturer and speaker, he had rare gifts and he was famous for his knowledge of biblical literature and Shakespeare. On one occasion he read the part of Macbeth in public, with Fanny Kemble reading that of Lady Macbeth. Walter Channing was twice married. He had one son, William Ellery 2nd, the poet, who died in Concord in 1901, and three daughters. He died July 27, 1876, at the age of ninety years and three months.

REFERENCES

Authorities chiefly consulted: (1) *Laing-Gordon, W.*: Sir James Young Simpson and Chloroform. New York, 1897. (2) The Late Dr. Channing: Boston Med. & S. J. 10: 237, 1876. (3) *Kelly and Burrage*: Am. Med. Biog., Baltimore, 1920. (4) *Channing, Walter*: A Treatise on Etherization in Childbirth, Boston, 1848. (5) *Channing, Walter*: Notes on Anhaemia, etc., N. E. Quar. J. Med. Surg., 157, Oct., 1848. (6) *Channing, Walter*: A Physician's Vacation, Boston, 1856. (7) *Harrington, T. F.*: The Harvard Medical School, New York, 1905.

NEW HAVEN HOSPITAL.

TUBERCULOSIS OF THE CERVIX*

BY BRUCE ALEXANDER HARRIS, B.S., M.D., F.A.C.S.

BROOKLYN, NEW YORK

(From the Department of Obstetrics and Gynecology, Long Island College Hospital)

WHEN we consider the large percentage of the population suffering from tuberculosis in some form or other, it is not surprising to find the genital system involved in a considerable number of these cases. Yet the identification of a pelvic

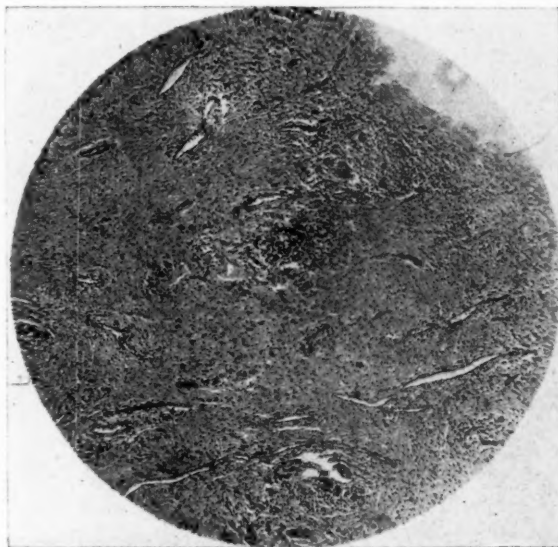


Fig. 1.—Section of cervix just beneath the portio. The stroma is infiltrated with moderate numbers of lymphocytes. Close to the area of ulceration is a large tubercle. The giant cells are prominent even under this magnification. $\times 80$.

lesion as tuberculous may not be made prior to operation. Frequently it remains for the pathologist to make the diagnosis. In cases, however, where the pelvic findings are associated with a known tuberculous lesion elsewhere in the body, the investigative procedures may be extended to rule out the possibility of a common etiologic factor.

Due to the insidious progress of this type of infection, and the tendency of the profession to fail to recognize tuberculous lesions of the reproductive system as such, a report of a case of cervical tuberculosis at this time might be justified.

*Read at a meeting of the Brooklyn Gynecological Society, March 7, 1930.

Primary cervical tuberculosis is exceedingly rare. In 1908 a very careful review of the literature on this subject resulted in only six cases of primary tuberculosis of the cervix. Cases reported by Klobb, Kaufmann, Michales, Broucha and Chaton, Brooks and Ferrari were accepted. Due to the quiescence or even resolution of the primary tuberculous lesion elsewhere in the body some of the above-mentioned carefully reviewed cases could still be secondary cervical lesions. While primary cervical tuberculosis is a possibility the lesion is generally considered to be secondary.

The clinical history of the patient forming the basis of this report is as follows: The patient, M. G., aged thirty-one, married, white, was referred from the Polhemus Clinic to the gynecologic wards of the Long Island College Hospital on Dr. Gibson's Service in November, 1924, with the diagnosis of a probable malignant lesion of the cervix. She complained of pain in the back and lower left quadrant of the abdomen, and of having frequent vaginal bleeding during the past two or three months.

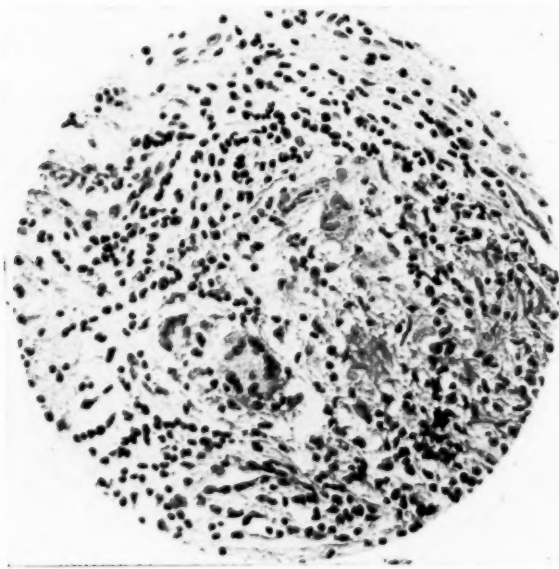


Fig. 2.—Structure of the tubercle is fairly well defined. The clear epithelioid cells and the giant cells are well shown in the center. At the periphery lymphocytes are numerous. $\times 120$.

One sister died at the age of 22 with "hasty consumption."

The past history was negative except for an operation eight years ago for retroversion of the uterus and a curettage three years ago for bleeding following a spontaneous abortion at the third month.

The menstrual and intermenstrual histories were negative up to the present illness.

The obstetric history records six full-term pregnancies and two spontaneous abortions. The last pregnancy occurred three years ago and terminated in a spontaneous abortion at the third month.

Complete physical and laboratory examinations revealed negative findings except for a weak general appearance, moderate oral sepsis, and x-ray diagnosis of old apical tuberculous lesions in the lungs, tenderness on deep palpation over both lower quadrants of the abdomen, a bloody vaginal discharge, an enlarged, eroded,

and tender cervix, a slightly enlarged uterus which was limited in motion and sensitive and tender adnexa and parametrium. The parametrium was not indurated.

A diagnostic curettage of the uterine cavity and a biopsy of the cervix was done. The pathologic diagnosis on these specimens was: *Interstitial tuberculosis of the cervix and subacute inflammatory endometritis.*

Later when the patient's general condition had been sufficiently improved, the uterus, tubes, and ovaries were removed by abdominal section. Careful pathologic study of these specimens showed that the tuberculous lesion was confined to the cervix alone, and that the supposed tuberculous involvement of the adnexa was a pelvic inflammatory disease of gonorrheal origin.

The patient made a good recovery and since leaving the hospital her general condition has greatly improved.

(For discussion, see page 275.)

de Udaeta y Bernareggi, A.: Phototherapy in Gynecology. Rev. Espan. de obst. y gynec. 14: 105, 1929.

In the main, this article deals with the physics of the ultraviolet ray. Its mode of production is discussed very thoroughly, as well as the various lamps constructed to produce it. Its value in promoting the general health of the individual, and its effect on the different systems of the body are also touched upon.

In gynecology, it has been found useful, especially where other means of treatment have failed, and also in conjunction with other therapy. Such conditions as pruritus, eczema, condylomas, and irritation due to discharges, are definitely benefited and often cured. Kraurosis, the leucoplakias, and lupus vulvae have also been improved. Affections of the vagina are not as amenable.

Cervical erosions which the usual medications have failed to clear up respond readily to ultraviolet light. It should be used here in preference to operation. Chronic metritis responds readily. For uterine bleeding, e.g., due to fibroids, the treatment is beneficial in promoting hemostasis, but x-ray is much more efficacious. In pyosalpinx the results have been excellent, especially in combination with diathermy. Good results also have been obtained in dysmenorrhea, menorrhagia, oligomenorrhea, genital hypoplasia, menopausal symptoms, and vaginal metrorrhagia. Contraindications to its use are acute conditions and high temperature.

Dosage depends upon skin sensitivity, determined by exposing small areas at a distance of one meter for from one to six minutes and noting the maximum time at which an erythema not too intense is produced. Very strong doses are necessary for the cervix.

FRANK SPIELMAN.

PURPURA HEMORRHAGICA COMPLICATING PUERPERIUM*

BY HENRY B. BOLEY, M.D., BROOKLYN, N. Y.

PATIENT G. F., white, twenty-four years of age, was first seen by me on April 2, 1929, because of amenorrhea.

Menstruation began at fifteen years of age, regular, every twenty-eight days, lasting from three to four days, moderate in amount, not associated with pain or any other abnormal symptoms. Last menstrual period January 12, 1929, was normal in all respects. On February 15, patient spotted for about half a day.

Married for one year, contraceptives used for short time; no history of profuse bleeding at time of defloration.

Physical examination negative. Pelvic measurements normal; no masses or bony obstructions noted; normal pregnancy of about twelve weeks; adnexa negative.

Blood pressure ranged from 120/70 to 112/68; urine negative throughout; never complained of any untoward symptoms. On August 27, blood pressure showed slight elevation to 136/90; urine negative; no signs or symptoms of impending trouble. Precautionary measures were instituted, however, and patient was requested to return at weekly intervals. Condition remained unchanged until September 30. At that time patient showed all the classical signs and symptoms of impending eclampsia, blood pressure elevated 190/120; urine boiled solid, many hyaline and granular casts, few red blood cells.

Patient was admitted at once to the Jewish Hospital on September 30, about 1 P.M. Examination revealed puffiness of eyes, anxious expression; peculiar mottling of skin of the face; accentuation second aortic sound; pregnancy about thirty-seven weeks, fetal ovoid showed back to left, small parts to right, vertex below and engaged, breech above; fetal heart L.L.Q., good quality. Rectal examination: cervix effaced, os admitted tip of finger, membranes intact, vertex in midpelvis. Although patient was not experiencing pain, distinct contractions were visible. In view of the above findings, conservative management was deemed advisable. Within twelve hours after admission cervix was fully dilated; head at the spines. Membranes were artificially ruptured, episiotomy performed, and low blades applied. Normal living female child delivered, weighing 4 pounds 7 ounces; placenta and membranes expressed intact, episiotomy repaired.

There being no appreciable bleeding, and because of the hypertension, no pituitrin or ergot was given. Light ether anesthesia was used.

Immediately after delivery blood pressure was 100/70; pulse good quality; general condition good. Within twenty-four hours all signs and symptoms of toxemia disappeared except for slight trace of albumin.

The first twenty-four hours of the puerperium were normal; no rise in pulse, temperature, or respiration. On October 2 ecchymotic spots were noted on the abdomen and under both knees, as a result of the expression of the placenta, and the pressure of the metal leg holders.

The following morning the patient had a severe nose bleed which was only checked after nasal packing was used. At the same time, a marked change in the lochia was noted; it was more profuse and bright red in color. The uterus was well contracted, and in spite of oxytocics employed, the lochia continued in profuse quantity. Blood pressure 120/70.

On October 4, with the appearance of numerous petechiae over the breasts, abdomen, arms, and mucous membranes, purpuric areas at the sight of hyper-

*Presented at a meeting of the Brooklyn Gynecological Society, March 7, 1930.

dermic injections, a medical consultation was held. A blood transfusion was advised and a blood study was requested. Patient was now showing signs of blood loss. Temperature, pulse, and respiration were all elevated. Spleen was palpable. Blood transfusion was given, 350 c.c. Blood examination: Hb., 35 per cent; R.B.C., 1,650,000; W.B.C., 23,100; platelets, 90,000; bleeding time over fifteen minutes; clotting time, three and one-half minutes; clot retraction, none in twenty-four hours.

Her general condition did not improve. Medical and surgical consultation held. Consensus of opinion, immediate splenectomy. Patient transferred to Surgical Service. Splenectomy performed by Dr. Wm. Linder. Spleen $2\frac{1}{2}$ times normal size, dark and congested, studded with ecchymotic areas. The peritoneum and all organs which were visible were full of petechiae. It was extremely interesting to note that no sooner were the splenic vessels ligated than all bleeding from oozing surfaces ceased at once. Patient stood operation very well. A transfusion of 500 c.c. of blood was given immediately after the operation.

On October 7 episiotomy wound was noted breaking down, two large ecchymotic pressure sores noted on either side of coccyx. Blood one day postoperative, Hb., 33 per cent; R.B.C. 2,030,000; W.B.C., 20,000; platelets, 250,000 (compared to 90,000 before operation); bleeding time, one-half minute; clotting time, four minutes; patient appears in better condition.

October 8 and 9 condition fair; patient comfortable; no new petechiae noted; lochia less profuse; bleeding from nose and gums stopped. Temperature fluctuating 100-102° F.

October 10 transfusion of 400 c.c. of blood given.

October 16 patient complaining of pain in left chest on deep respiration; temperature 103°; pulse 120; respirations 28. Few moist râles at left base.

October 17, more definite signs of fluid and consolidation at left base.

October 19, patient toxic; temperature 105°; some cyanosis; x-ray revealed diffuse opacity at left base indicating pleural reaction with fluid; aspiration performed, 50 c.c. of straw-colored fluid removed.

October 20, patient getting progressively worse; appears septic; temperature 104°; blood culture sterile; extension of pulmonary signs over right middle lobe. Slight infection of operative sight.

October 21 patient died.

Baby was discharged from hospital in good condition and up to present time has shown no signs of the disease.

Pathologic report: spleen slate-colored, hard, enlarged $2\frac{1}{2}$ times normal; several ecchymotic areas on surface. Microscopically, moderate fibrosis with areas of hemorrhage.

This case is reported not because of the purpura hemorrhagica, although that condition is in itself a rare one, as is pointed out by Rushmore* in his review of this subject, but because of the fact that this symptom complex only manifested itself on the third day of the puerperium.

This case must naturally bring up the question as to the relationship of toxemia of pregnancy to purpura hemorrhagica complicating pregnancy and the puerperium. In the majority of cases reported, this condition was associated with some signs of toxemia. The case reported here is probably a case of latent purpura which was aggravated by the change in the metabolic processes or the toxins produced by the impending toxemia. As to the rationale of the treatment, I am of the opinion that this patient would have recovered from the splenectomy were it not for the complicating pulmonic infection which set in and caused her death.

205 HICKS STREET.

*AM. J. OBST. & GYN. 10: 553, 1925.

ANEMIA IN PREGNANCY

A FINAL REPORT ON THREE HUNDRED OBSERVED CASES

By JOHN H. MOORE, M.D., F.A.C.S., GRAND FORKS, N. D.

IN THE AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY for September, 1929, I made a preliminary report on 100 pregnant women upon whom routine blood examinations had been made to determine the average hemoglobin readings and the average red blood cell counts.

This work has been continued, following the procedure as outlined in the original article, and Tables I, II, and III are based upon a study of the 300 observed cases:

TABLE I

NUMBER OF CASES	AVERAGE HG.	AVERAGE R.B.C.
300	79%	4,342,610

TABLE II

	NUMBER OF CASES	AVERAGE HG.	AVERAGE R.B.C.
Primiparae	135	79.2%	4,447,798
Multiparae	165	78.7%	4,304,086

TABLE III

Age	50 OR LESS	50-60	60-70	70-80	80-90	90 OR ABOVE
Number of cases	3	18	28	103	116	32

The major complications encountered in this series are of interest: nephritis complicating pregnancy occurred in 10 cases; preeclamptic toxemia in 2 cases; eclampsia in 1 case; pyelitis of pregnancy in 2 cases; mitral stenosis in 2 cases; acute polyhydramnios in 2 cases, and syphilis in 4 cases.

CONCLUSIONS

1. In 300 observed cases taken consecutively from my private obstetric practice the average hemoglobin reading was 79 per cent, and the average red blood cell count was 4,342,610. This is unquestionably lower than the commonly accepted average for normal, nonpregnant women.

2. The lowest average readings occurred in the group of cases having nephritis as a complication of pregnancy; the patients with syphilis showed a lower average in red blood cells than the average of the series, but with practically no change in the hemoglobin average from that of the entire series.

3. No wide variation exists between multiparae and primiparae in either hemoglobin readings or red blood cell counts in this series.

4. Excluding all cases of gross pathology, fully 50 per cent of the patients of this series showed a reduction in hemoglobin readings and red blood cell counts sufficient to place them in need of therapeutic measures to combat the secondary anemia.

I am again indebted to Mrs. Helen G. Korstad, laboratory technician, for the hemoglobin determinations and red blood cell counts on the patients in this series.

NORTHWESTERN NATIONAL BANK BUILDING.

FATAL BRONCHIAL OBSTRUCTION IN THE NEWBORN

BY PAUL C. LANGAN, M.D., AKRON, OHIO

IT IS the purpose of this paper to report what I believe to be a heretofore undescribed cause of death in the newborn baby. Although the mechanics involved and a somewhat similar course of events have been seen repeatedly and reported in older patients suffering from foreign bodies in the air passages, I have been unable to find a report of a similar death in a newborn, although the mechanism is simple and the danger always present.

Numerous cases have been observed of a foreign body in a major or main stem bronchus in which the foreign body has been present for a sufficient time to pass through the stage of obstructive emphysema described by Manges, to reach the stage of obstructive atelectasis, and in which the foreign body is finally dislodged in some manner and failing to be expelled through the trachea by the first expiration, it follows the only air current downward and plugs the opposite main stem bronchus, with a fatal result. This has happened in attempt at bronchoscopic removal in which the foreign body has either been fragmented or has slipped from the grasp of the forcep, and is one of the most tragic complications of endoscopy. It has often happened spontaneously in cases where for some reason or other endoscopy has not been done.

In the case to be reported, Mrs. S. S., white, aged thirty-nine, para ix, at full term in an uncomplicated pregnancy was admitted to the hospital at twelve noon and placed in a room. Pains were every two minutes, the membranes had ruptured before admission and on admission a note was made of mucous discharge and the fact that there was no "bulging." The patient was prepared hastily and was being taken to the delivery room at 12:25 when a 4.2 kg. girl was born precipitately on the stretcher. The infant cried, showed no jaundice or other abnormalities and was placed in the nursery. It did very poorly, became cyanotic and dyspneic and lost weight rapidly, on the fourth day weighing 3.4 kg. Because of its condition it was then transferred to the Pediatric Ward and was referred to the x-ray department with suspicion of, and a request for treatment of a pathologic thymus. The x-ray report was, that no thymic pathology existed and that the left main stem bronchus was occluded either by a congenital stricture or some foreign body, nonopaque, probably mucus, causing a left side atelectasis. The infant was in an extremely poor condition and at about 11:00 A.M. of its sixth day of life, was given 20 c.c. whole blood intraperitoneally. Twenty minutes later it became very cyanotic and died.

The conclusion was that the foreign body, or a portion of it, had become dislodged and had followed the air current into the opposite bronchus, causing death.

This belief was substantiated by the postmortem findings of a plug of mucus in both the main stems of the bronchi which was classified by the pathologist as, in his opinion, not of respiratory tract origin.

Although this case is unusual in that the cause of death was accurately established, the circumstances leading to it are most commonplace, and it serves to demonstrate the value of the time-honored teaching that the first duty of the obstetrician is the removal of any secretion from the upper air passages of the newborn babe at the earliest possible moment. It is my belief that this condition would be found more often at postmortem if not only the trachea but the entire bronchial tree were carefully laid open.

ST. THOMAS HOSPITAL.

THE USE OF A TOURNIQUET FOR THE CONTROL OF THE ABSORPTION OF SOLUTION OF PITUITARY IN THE INDUCTION OF LABOR*

BY SAMUEL HANSON, A.M., M.D., STOCKTON, CALIF.

(From the San Joaquin General Hospital)

THE indications for the use of solution of pituitary in obstetric practice are at present sharply limited to the third stage of labor. In the leading clinics it is seldom used in the first and second stages, and only occasionally for the induction of labor. The well-known objection to solution of pituitary is its tendency to produce excessively powerful and even tetanic contractions of the uterus. If these dangerous potentialities of the drug could be reduced, its usefulness in obstetrics would be greatly extended.

In order to gain some control over the action of solution of pituitary, Hofbauer¹ recently proposed an intranasal method of administration. His procedure consists of the application to the inferior turbinate of a pledget of absorbent cotton saturated with solution of pituitary. It is thus possible, if necessary, to terminate promptly the absorption of the drug, by withdrawing the cotton pledget from the nasal cavity.

It occurred to me that the advantages of Hofbauer's method can be secured by other means, without resorting to the slow and rather uncertain absorption through a mucous membrane.

The method recommended is very simple: the absorption of the drug is controlled by means of a tourniquet applied above the point of injection.

In detail the procedure is as follows:

The patient's blood pressure is taken. The cuff of the sphygmomanometer is applied at the wrist and inflated up to a pressure just above the patient's systolic blood pressure. Three-tenths c.c. of the solution of pituitary (10 international

*Read before the California Northern District Medical Society at Stockton, Calif., April 8, 1930.

units per c.c.) is injected hypodermically below the level of the cuff. The pressure is then released for thirty seconds and reapplied for two minutes, alternately, for a period of twenty minutes. The rate of absorption is thus reduced to one-fifth of the normal rate. If the pains do not become excessive in strength or frequency by the end of the initial period of twenty minutes, it is safe to release the pressure permanently. However, should excessively powerful contractions develop at any time during the above period, constriction is immediately reapplied and is henceforth maintained for intervals of as long as ten minutes alternating with periods of relaxation of only ten seconds. In this manner absorption may be almost completely interrupted for half an hour or longer depending on the indications. The above procedure is, of course, very flexible. By varying the length of the intervals of constriction and relaxation it is possible to control the rate of absorption sufficiently to satisfy almost any requirement, provided the initial dose of the drug is a reasonable one.

The time intervals as above recommended were derived from a series of 36 clinical tests performed on 25 patients past term, or in the beginning of the first stage of labor. Two-tenths to 0.5 c.c. of solution of pituitary was injected hypodermically and the tourniquet released periodically. The duration and frequency of the pains were timed carefully. These experiments showed that solution of pituitary is absorbed with great rapidity. If an effect was produced at all, in every instance it was obtained with an absorption time* of one and one-half to three minutes. Consequently, if the tourniquet is to be used effectively the intervals allowed for absorption must be very short—not longer than 30 seconds. It was also found that if the pains do not become excessively strong with an absorption time of 4 minutes, overdosage from further absorption need not be feared, and the constriction may be permanently released.

The pressure is applied at the wrist for the reason that it causes much less discomfort there than it does higher up on the arm. In fact, it was a revelation to find how easily continuous and complete interruption of the circulation can be tolerated at the wrist for periods of ten minutes at intervals of ten seconds, for half an hour or even longer.

The principle on which the method is based is, of course, not new. A familiar example is the intermittent application of a tourniquet to an extremity to retard the absorption of the poison in cases of snake bite. The principle of temporary circulatory interruption is, however, especially applicable to solution of pituitary, since the action of this drug is of relatively very short duration.

The present method is offered primarily as an aid to the induction of labor. It is not intended to give a sense of security or encouragement for the indiscriminate use of the drug in the first and second stages of labor. The method proposed is especially recommended in Watson's procedure,² which consists of a preliminary sensitization of the uterus with castor oil and quinine, and the subsequent administration of solution of pituitary in 0.5 c.c. doses every thirty minutes† for

*The phrase "absorption time" is used to designate the total length of a group of intervals during which absorption is allowed to take place. For example, if the constriction is released for thirty seconds every two minutes for a period of fifteen minutes the absorption time is three minutes.

†The dose at present generally recommended is 0.3 c.c. or less. In adopting the present technic to Watson's method, the injections should be given forty-five minutes instead of thirty minutes apart, to allow for the time lost during the intervals of constriction.

6 doses. The method may also be applied where solution of pituitary is indicated as an adjuvant to the induction of labor with the hydrostatic bag.

REFERENCES

- (1) *Hofbauer, J. I.*: J. A. M. A. 89: 24, 1927. (2) *Watson, B. P.*: AM. J. OBST. & GYNEC. 4: 603, 1922.

1009 MEDICO-DENTAL BUILDING.

A DIRECTOR FOR THE VAGINAL OCCLUSIVE PESSARY*

BY MAX D. MAYER, M.D., NEW YORK

(Adjunct Gynecologist, Mt. Sinai Hospital)

THE recent change of attitude toward contraception, where contraception is indicated, has in some degree outstripped the improvement in efficacy and applicability of available contraceptives. The renewed interest and more widespread use of the Mensinga (or Ramses) type of pessary has drawn attention to certain difficulties in its use.

Four troublesome features are: (1) the occasional difficulty, or even impossibility, of placing it in the correct position with the upper edge in the posterior fornix; (2) the occasional uncertainty on the part of the wearer as to its exact position; (3) the necessity of manipulation and fingering with the present technic of introduction; (4) the time and patience occasionally required of the doctor in instructing the patient.

These objections seem to have been adequately met by the use of the simple instrument I have devised,¹ which is pictured below.

This is an applicator or introducer, shaped like an elongated "S," and not unlike a tongue depressor. It is made of aluminum, and is seven and one-half inches long, three-quarters of an inch wide, and one-eighth of an inch thick, and has at one end a finger-like thickening, at the extremity of which is a transverse groove (Fig. 1). Into this groove fits the thick rim of the vaginal diaphragm, which is then stretched over the superior surface of the rod and held in a taut position by the thumb of the patient, whose forefinger is at the outer end of the instrument (Fig. 2). The lubricated diaphragm is then pressed into the vagina with one simple sweep of the hand, and automatically directed to its proper position by the shape of the instrument (Fig. 3). The instrument is then withdrawn (Fig. 4) and does not catch or dislocate the pessary. It is recommended not only for those patients who simply cannot place a pessary without it, but for routine use with this

*From the Committee on Maternal Health.

¹This director has been made for me by the Durex Products, Inc., 156 Fifth Avenue, New York City.

type of pessary. It will eliminate the difficult contraceptive problem presented by the very long vagina with cervix pointing far backward.

It is possible to use a tongue depressor, but this may cut the rubber and it lacks the curve that enables the cup to pass the projecting cer-

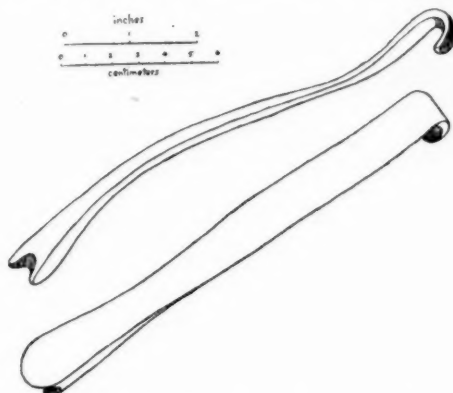


Fig. 1.—Director for placing pessary.

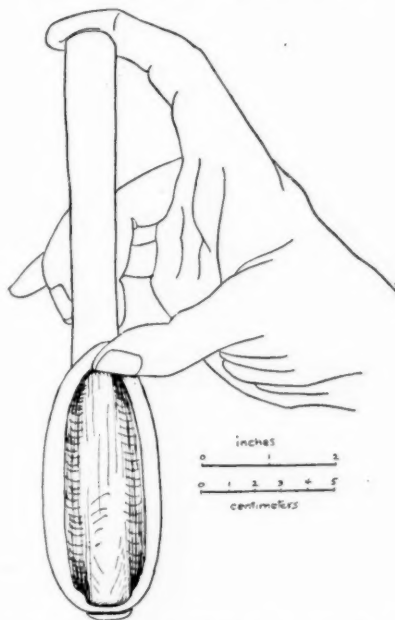


Fig. 2.—Insertion of pessary with aid of director.

vix by hugging the posterior vaginal wall. The applicator formerly sold by dealers, which is an incurved lateral compressor, adds to the bulk of the mass to be introduced and is inelastic so that rigid metal and not compressible rubber must be pushed past the entrance into the vagina.

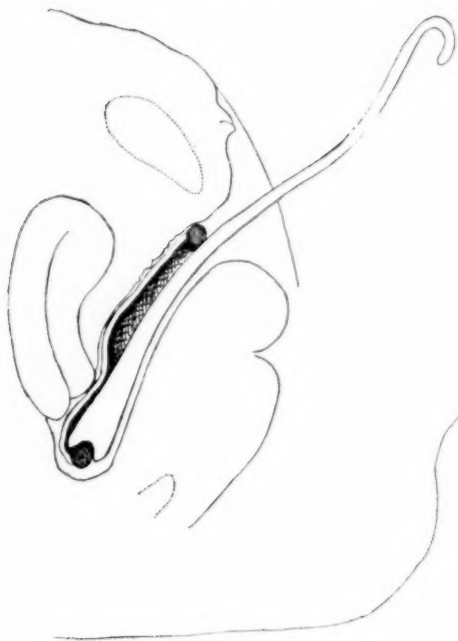


Fig. 3.

Fig. 3.—Cross-section of body showing director placing farthest part of circle of pessary beyond cervix.

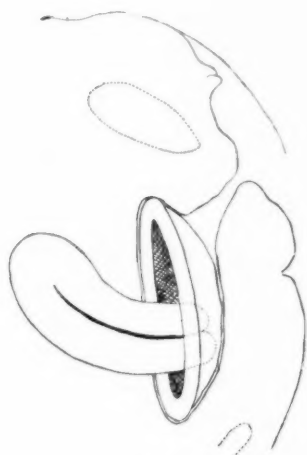


Fig. 4.

Fig. 4.—Correct placing of pessary. Anterior bar well caught behind subpubic arch. Cervix is covered.

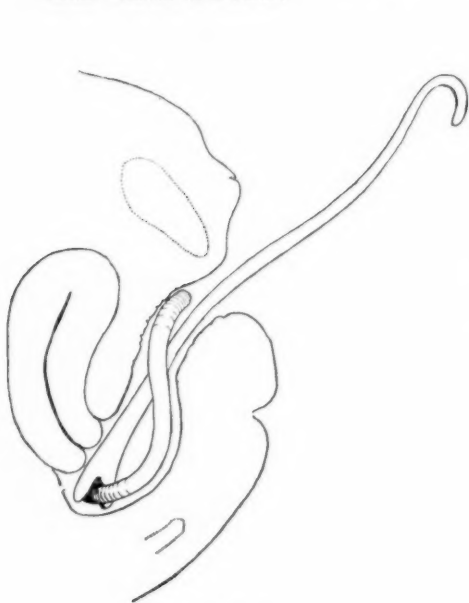


Fig. 5.

Fig. 5.—Director placing farther rim of Smith pessary beyond cervix into posterior fornix.

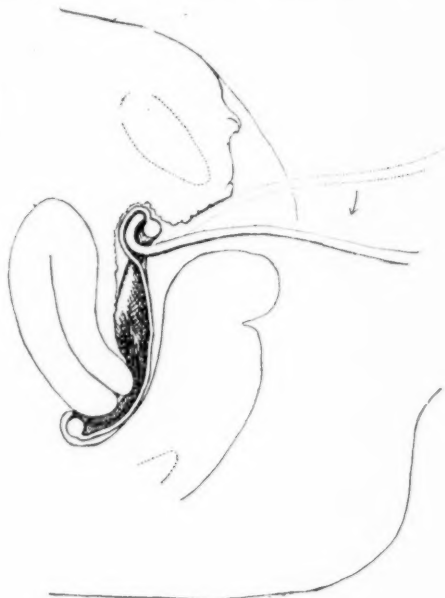


Fig. 6.

Fig. 6.—Use of director to remove pessary.

The same device (Fig. 5) enables wearers of Smith or Hodge pessaries to remove and replace them, in those cases where removal does not dislodge or displace the repositied uterus. It is an efficient substitute for the gynecologic finger, of which it exactly duplicates the mechanism and action.

For removal of either the contraceptive diaphragm or the Smith pessary, the end opposite the grooved tip bears a blunt hook with a curve adapted to the thickness of the usual pessaries (Fig. 6). As a well-fitting pessary of either variety sits rather snugly up behind the pubes a patient sometimes finds difficulty in seizing this anterior extremity with her finger to draw it downward and backward before withdrawal. The instrument constitutes an extension of the hooked finger and its use is obvious as shown by the diagram (Fig. 6).

Instruction in the use of the instrument takes far less time than the reading of these few lines. My own experience with instruction shows that one demonstration of placing and removal suffices.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF MARCH 11, 1930

DR. J. H. TELFAIR presented a report on **Complete Inversion of the Uterus During Labor**, and said that this was the second case where he reinverted the uterus by simply pushing it up into the pelvis, and in each case it was rather easy to replace the uterus in normal position through the noncontracted cervical muscle fibers.

DISCUSSION

DR. A. M. JUDD.—I have seen but two cases of inversion of the uterus. One was acute and the patient died within a few minutes after I reduced it. The other existed for nine months after its occurrence. The patient was extremely anemic and in that case I did a Spinelli operation. The patient recovered and subsequently had a baby after that normally.

DR. ELIOT BISHOP.—I have seen only one case of inversion of the uterus, five or six hours after delivery and in some shock. The patient was referred to the hospital after delivery at home. At that time the Spinelli was the operation of choice, unless the uterus could be easily resposited, and not being able to reduce the uterus in that case I attacked it by the Spinelli method, and the patient died on the operating table.

A newer and better method of attack is described by Huntington, Kellogg and Irving, of Boston, in an article published by them in the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY* 15: 34, 1928. Their practice is to immediately transfuse the patient to combat shock, the major problem, and do a quick laparotomy; the inversion is reduced in the reverse order of occurrence, using Allis clamps. This is much more simple than the complicated Spinelli procedure, which also invades the peritoneal cavity, though from below.

DR. EDWIN W. HOLLADAY described the **Repair of an Intractable Vesicovaginal Fistula**. The successful, complete cure of this case was felt to be due to several minor points in technic and for that reason it is presented.

The patient, Mrs. M. P., Greek, thirty-one years of age, para v, was about five feet tall and weighed 155 pounds. Her family history and previous medical history had no bearing on the present condition.

Her present complaint began five years ago following the birth of her fourth child, since which time she has had incontinence of urine. During this time she has undergone five unsuccessful operations by different operators in other cities. Three of these operations were vaginal, one was suprapubic, and one was an attempt at vaginal followed by a suprapubic operation. Following the first operation a diagnosis of bilateral renal tuberculosis was made from cystoscopic examination. In addition, following the third operation a cesarean section was done, most likely because of the fistula and the extensive scar tissue present. She had thus undergone six operations in less than four years. She was admitted to Bellevue

Hospital September 23, 1929, complaining of complete incontinence of urine. Physical examination showed a very adipose female, thirty-one years of age, not acutely ill. The abdomen showed very dense and extensive scars in the suprapubic region. There was a relaxed parous pelvic floor. The entire vulva was badly excoriated. The cervix was high up and fixed by very extensive scar tissue. The fundus was retroverted and not well palpated, due to scar tissue. On the anterior wall there was a fistula admitting almost three fingers, so that the contracted bladder could easily be palpated with the examining fingers. The fistula was just behind the proximal end of the urethra and measured about $1\frac{1}{2}$ inches in diameter. It was located more to the right side, lying very close to the right ureteral orifice. Bladder mucosa could easily be seen running into the extensive scar on the anterior lip of the cervix. While the patient was being studied she was kept in bed, and efforts were made to improve the local condition of the tissues. She was operated upon October 31, 1929 in the gynecologic service of Bellevue Hospital.

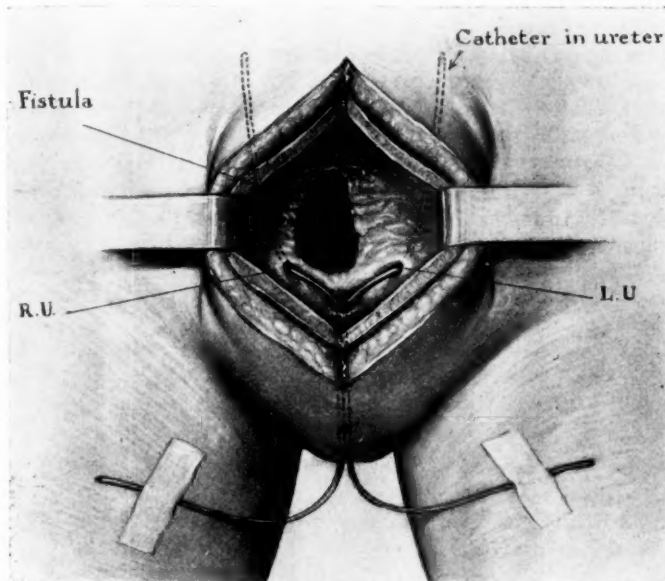


Fig. 1.

A longitudinal incision was made through the dense suprapubic scar, and the peritoneal cavity was intentionally opened to facilitate identifying the contracted bladder bound up in the thick scar tissue. The bladder was located and incised. With the use of Deaver retractors and the Cameron light the ureters were located and No. 6 catheters inserted 15 cm. within the ureteral orifices. An endoscope was passed and the ends of the catheters were brought out through the urethra and fastened to the thigh. The bladder wound was covered over and left open while the vaginal repair was being done. A Schuchardt paravaginal incision was made on the left side to make the fistula more accessible. The cervix was grasped with a tenaculum but could not be pulled down. Scar tissue around the edge of the fistula was excised. The vaginal mucosa was separated. With great difficulty the bladder was mobilized as much as possible around the periphery of the fistula from the surrounding scar tissue. On the right side, due to the proximity of the right ureter, very little free bladder edge could be obtained. At this point the catheter in the ureter fortunately saved us from cutting the ureter. The scar

tissue on the mobilized bladder edge was then excised. It was then seen that in spite of as wide mobilization as could be obtained it would be impossible to use the usual interrupted sutures in the bladder. A purse-string suture of No. 0 catgut was passed around the bladder opening and the edge inverted into the bladder as it was tied. A second purse-string suture of No. 1 chromic catgut was passed outside of the first suture. A third similar purse-string suture was then passed. Interrupted chromic sutures were then placed in the fascia to reinforce the bladder closure. Some scar tissue in the vaginal mucosa was then excised and the edges brought together with interrupted chromic sutures. The Schuchardt incision was closed with interrupted sutures in layers. The bladder was then inspected through the suprapubic wound and the catheters were found in place and the fistula site well closed. The bladder was closed by interrupted sutures. A mushroom catheter was inserted and fastened with a purse-string suture. The muscle and fascia were closed with interrupted sutures and the skin approximated with silkworm gut.

Aftertreatment: The ureteral catheters were left in place for six and seven days respectively, being irrigated every three hours with 1:5000 acriflavine. The suprapubic catheter was connected with a bottle and irrigated twice a day with acriflavine. It was removed on the tenth day and the wound gradually healed. The patient was discharged twenty-one days later, on November 21, in good condition. At the return clinic in January she was found to be completely healed, with no fistula and no leakage. She states that she can easily retain her urine for several hours without distress and that her capacity is increasing.

Summary: 1. After five previous unsuccessful operations the patient was completely cured by a combined suprapubic and vaginal operation.

2. Suprapubic insertion of ureteral catheters was feasible even when insertion by urethra was impossible.

3. Purse-string sutures of the bladder opening were utilized where interrupted sutures were impractical.

4. Ureteral catheters were left in place for six days without harm to the patient.

5. Combined suprapubic drainage and drainage by ureteral catheters kept the bladder dry, allowing union to take place.

DISCUSSION

DR. F. C. HOLDEN.—This combined suprapubic and ureteral catheterization was done years ago by Kelly.

Our patient was in the ward about a month before we attempted to do anything about it, and we gave her a good deal of consideration. We have treated another similar case, not similar in the size of the fistula, but in the fact that she had been operated upon six times for an intractable fistula. That patient was operated upon by this same procedure and we are quite sure we have cured her.

DR. H. D. FURNISS.—Two points are worthy of discussion. One is that the bladder can be opened transperitoneally without much danger of peritonitis; in fact, some of the German operators have deliberately repaired many of these vesiovaginal fistulas by the transperitoneal operation, instead of doing it suprapubically and extraperitoneally.

Another point in technic is that if the operator does not want to enter the peritoneum from above, he can make an incision in the bladder transversely and enlarge it to any degree without danger of cutting the peritoneal reflection and entering the peritoneum.

DR. HOLLADAY (closing).—I desire to correct the impression of Dr. Furniss that this bladder was attacked transperitoneally. The peritoneal cavity was en-

tered just to allow of the bladder being located. The scar tissue was so dense that it was just like cartilage for two inches in breadth. After the bladder was opened the peritoneal cavity was closed.

DR. ROBERT T. FRANK read a paper entitled **Progress in Endocrinology of Interest to the Gynecologist and Obstetrician.** (For original article see page 215.)

DISCUSSION

DR. W. H. CARY.—I would like to ask if the female sex hormone would be effective in helping certain cases of sterility in which probably there is a failure of the ovum to become implanted and nourished by the endometrium. If I understood him correctly, the female sex hormone does cause hypertrophy and congestion of the uterus.

I would also like to ask if the endometrium possibly has some direct or indirect hormone action.

DR. R. T. FRANK.—Dr. Coe mentioned a very interesting group of cases where development has lagged behind. We see two types of these, those in which no signs of puberty occur, individuals who are almost eunuchoid, in whom the secondary sex characteristics have not developed; others who are typically feminine, who have well-developed breasts, hair distribution, larynx, fat distribution, etc. In the former we do not expect, and do not find any evidence of ovarian activity, as far as our investigations go, but in the others, although they may never have menstruated, we do find the hormone in the blood in some cases. Several cases are on record of patients who have never menstruated and have had children.

Dr. Cary has brought up a very interesting phase of sterility, the investigation of which is only in its infancy at present. The subject is so vast that it is impossible for me to enter into any sort of details here. I merely want to say that in gauging and evaluating sterility there are a number of possibilities; for example, ovum production may be defective; in the next place, the uterine endometrial reaction may be defective in two ways, in the one that the necessary pregravid change does not take place. Some very recent work of Corner's is very illuminating in this regard. He feels that the aqueous extract of the corpus luteum, to which I referred, is the extract which produces the endometrial change. I believe that the work of Allen and Pratt and that of others who have worked on monkeys and who are able to get a pregravid change in the uterus of a castrated monkey with nothing but the female sex hormone is incontrovertible. On the other hand, Corner has demonstrated one thing beyond doubt; he has been able to remove the corpora lutea in impregnated animals before the ova have reached the uterus and has allowed them to imbed and reach maturity, normal labor eventually taking place, by the exhibition of this aqueous extract of the corpus luteum, a problem which had previously baffled all investigators.

The beginning of the modern endocrinology is really based on the work of Born and Fränkl, who showed that the corpus luteum was necessary for nidation, and no means was found until the extract of Corner's was obtained in making the ovum take root unless the corpus luteum was present. That is not controverted by the fact that after the ovum once has taken root the corpus luteum can be removed, but in order to imbed, the corpus luteum secretion is necessary.

DR. F. E. KEENE AND DR. R. A. KIMBROUGH, JR., of Philadelphia, read a paper (by invitation) entitled **Fibromyoma Uteri, Treatment and End-Results.** (For original article see page 198.)

DISCUSSION

DR. W. P. HEALY.—It is quite impossible, in my opinion, to take issue with any of the statements in this report, which represents a sound and sane deduction from actual experience as we see it today in the treatment of this benign lesion in the uterus.

There are one or two points that stand out which may possibly be worth emphasizing, one of which is the treatment of the patient suffering from anemia as the result of her myomas, in which you feel that you would prefer a surgical method of approach, but it is quite out of the question to begin in that way because of the anemia. We have found that the preferable way to get the patient in condition for surgery is by the use of the roentgen ray. We do not attempt to approach the treatment of that type of case with intrauterine application of radium, and it is very interesting to note that even an extremely large tumor will occasionally diminish so appreciably in size that within a short time, two or three months, while the patient's general health is improving, you may begin to doubt the necessity of carrying out the surgical procedure that was originally contemplated. This improvement is brought about entirely without the use of transfusion or any other form of therapy except certain medical measures and the use of the roentgen ray.

Then as to the association of malignant changes in the uterine endometrium with the presence of myomas: I have emphasized a good many times, and I still think it most desirable to do so, that the risk of a mistake in diagnosis is not in the younger woman before the age of the menopause, but is in the woman after the menopause who is found to have uterine myomas and who has again begun to bleed. That woman is seldom bleeding from myomas; she is nearly always bleeding from cancer of the corporeal endometrium and should not be treated by radiation therapy in any form, unless diagnostic curettage is first carried out to clear up the question of malignant change complicating the myomas.

It is interesting to note the infrequency with which we meet sarcoma in the uterus since we have been using radiation therapy for the treatment of myomas. I am of the opinion that many of these cases of sarcoma of the uterus, which develop, as you know, more often from the benign myoma than from the uterine musculature, are radiosensitive, and that, in all probability, in treating cases of bleeding uteri which we assume are due to myomas, we are now curing a certain number of cases of sarcoma.

DR. H. C. COE.—Dr. Healy emphasized an important point when he said that we should never lose sight of the fact that a patient with myomas may have a beginning carcinoma of the fundus. That has been impressed on my mind several times, once as a most unexpected result of a curettage in a case with no symptoms pointing to malignant disease. The pathologist reported an early adenocarcinoma. I operated upon that patient twelve years ago and she is well today. Two years ago at the Woman's Hospital I had a woman fifty-one years of age, who was in perfect health, but had a history of irregular bleeding. She had an interstitial fibroid of the fundus and, naturally, I thought that the bleeding was due to that condition. I curetted her and applied 1200 mg. hr. of radium. The report from the pathologist did not come in until after she had left the hospital. It was adenocarcinoma. She had a prolapse of the rectum and I persuaded her to return so that I could do a Whitehead operation. I not only did the Whitehead but took advantage of the opportunity to perform a vaginal hysterectomy at the same time. She was so much interested in the rectal condition that she never knew anything about the hysterectomy until later. She reports regularly and is in perfect health.

DR. W. T. DANNREUTHER.—In the first place, I would suggest that a latent salpingitis constitutes more than a contraindication to radiation. It should be regarded as a real hazard, whether coexisting with a myoma or in the presence

of carcinoma. In three instances in my experience radiation has been followed in less than thirty-six hours by acute pelvic peritonitis; twice in cases of carcinoma, and once in a case of fibroma. In all three of these, the patients were carefully examined to exclude the presence of a latent tubal infection, and no evidence of salpingitis could be found on palpation. However, it must have been present. All of my patients recovered, but one of my colleagues in the Post-Graduate Hospital had a similar experience and the patient died.

I was particularly interested in the mention of eight patients in whom myomectomy was done, none of whom became pregnant. The more I review my past experience with myomectomy, the less I am inclined to utilize it in the future. I performed a hysterectomy last week on a patient on whom I did a myomectomy six and a half years ago, and in the past twelve months I have reoperated upon three other patients, all of whom had had myomectomies five or more years previously.

My experience parallels that of the essayist; I have not observed a single patient on whom I have done a myomectomy who became pregnant afterward. This may have been simply my misfortune; or perhaps I have not done enough of them.

I also desire to suggest that a gynecologist who has had a reasonable experience with radium therapy, and who adapts his dosage and filtration to the size of the uterus, the amount of bleeding, the vital resistance of the patient, and takes into consideration all other factors which may be of importance in estimating the proper dosage, can use intrauterine radium therapy in the treatment of small intramural bleeding fibroids, even in the woman of childbearing age, with satisfactory results and without inducing a premature menopause.

DR. E. T. HULL.—I would like to say a word in favor of myomectomy during the childbearing period because my experience has been different.

I can recall three cases in the last three years where I have done a myomectomy and have subsequently delivered the patient in each instance.

I feel that there are too many uteri taken out of young women, and it is surprising to me that when you start out to enucleate one fibroid after another, you find, when you get through, that you have a pretty good uterus. The most striking case I have in mind was one in which I removed thirteen fibroids from the uterus of a young married woman. On opening the abdomen the pelvis was found filled with a mass of nodules, ranging in size from an English walnut to that of a lemon. It did not look like much of a uterus, but she was very anxious to have a baby, so I enucleated the fibroids and inside of a year she was pregnant and I delivered her. Another case I have in mind was that of a sterile woman who had been married twelve years. She had a history of long-continued menorrhagia. Three curettages had been done and I did a fourth with permission to open the abdomen if I found reason therefor. On the posterior wall of the uterus there was a convexity. I split the posterior wall of the uterus and enucleated a fibroid the size of a hickory nut. Inside of three months the patient became pregnant and I delivered her at full term.

I believe many of these uteri are removed where they could very well be enucleated of their fibroid growth, even multiple fibroids, and when this is done many of them, in my experience, become pregnant.

DR. H. B. MATTHEWS.—I would like to know if Dr. Kimbrough always conserves the ovary within the pelvis or transplants it after the method of Blair-Bell, in the rectus muscle, or inguinal canal, or some other suitable place.

DR. R. T. FRANK.—About fifteen years ago I gathered 500 cases of fibromas among which 20 per cent were treated by radiotherapy. Some ten years later Lockyer of London, published 500 cases in which his percentage was around 19.5, if I remember rightly. The only point that I would like to bring out is that al-

though we used radiotherapy in 20 per cent, in a huge majority of these, x-ray instead of radium was used, showing that the radio activity is really the important factor rather than the method by which it is applied.

Like Dr. Dannreuther, I use myomectomy less and less, but in extenuation I wish to say and to emphasize the fact that the nature of the speaker's paper prevented him from suggesting perhaps as clearly as he might have desired that many fibroids require no treatment. In 50 per cent of fibroids of my series I found that no intervention of any kind was required, and I think, for the guidance of the general practitioner, that this fact should be emphasized more and more, because patients are very much disquieted by being told that they have fibroids and then they go around for specialistic advice which very often is extremely varied in its character.

DR. A. W. BINGHAM.—I would like to ask the doctor why radium was used more than the x-ray, particularly when the x-ray is simpler and gives us uniformly good results.

DR. KIMBROUGH (closing).—In reference to conservation of the ovary, I would say that almost without exception we conserve the ovary in its original site; its blood supply there is natural, and we feel this is followed by better end-results. Occasionally an indication will arise for implantation by the method of Blair-Bell into the rectus muscle. In this series the ovaries were all conserved in situ.

In reference to the use of radium in a large number of cases: we feel that diagnostic curettage is indicated in all cases and should be carried out, unless there is a definite contraindication to anesthesia. While we have the patient under anesthesia we prefer to give a simple treatment which is over in twelve to eighteen hours rather than to have the patient come in for diagnostic curettage and remain in the hospital four or five days for that, and then come back six, eight, or ten times for x-ray treatment later on. It is merely a question of conservation of the patient's time, and makes for simplicity.

PHILADELPHIA OBSTETRICAL SOCIETY

MEETING OF FEBRUARY 6, 1930

DR. GEORGE M. BOYD reported two cases of **Extrauterine Pregnancy at Full Term.**

CASE 1.—Mrs. A., colored, aged twenty-six, had had two children without difficulty. She was admitted to the waiting ward of the Philadelphia Lying-in Charity December 21, 1895, in the last month of gestation. The child was found to be in a transverse position, and an unusual proximity of the fetal membranes to the abdominal wall was noted, the pulsating umbilical cord being detected through the skin. The uterus could be felt above the pubic symphysis and it was the size of a twelve weeks' pregnancy. The patient's pulse and temperature were normal and she had little discomfort until January 16, the date fixed for her delivery. Then suddenly, the child died, and she complained of a colicky pain about the umbilicus. Her pulse, which heretofore had been normal, became very rapid, and operation was imperative.

Operation January 18, 1896. Under anesthesia, the uterus could be better outlined; the depth of its cavity was 9 cm. and it contained clots and decidual tissue. An incision along the outer border of the right rectus muscle revealed the fetal sac adherent to the parietal peritoneum. On incising the sac, there was profuse hemorrhage and a dead macerated child was extracted which weighed 3250 gm. (7¼

pounds). The uterus was now found to be posterior to the sac. The pregnancy had evidently had its origin in the right tube, primarily, and the placenta was implanted on the posterior surface of the broad ligament and extended over the pelvic cavity and uterus. Hemorrhage was now so pronounced and the patient's condition so serious that no attempt was made to separate it. The fetal sac was firmly packed with gauze and the patient stimulated, but the same day she died of hemorrhage and shock.

CASE 2.—Mrs. W., colored, aged twenty-one and a primipara, was admitted to the Graduate Hospital, April 25, 1929. Her last period came on August 1, 1928, and continued for three days. In October, about two months after this date, she developed considerable pain in the right lower abdomen and she called in her physician. She states that she remained in bed one week when the symptoms disappeared. At this date the pregnancy probably became abdominal. She never had any bloody discharge and had little discomfort. At the eighth month of

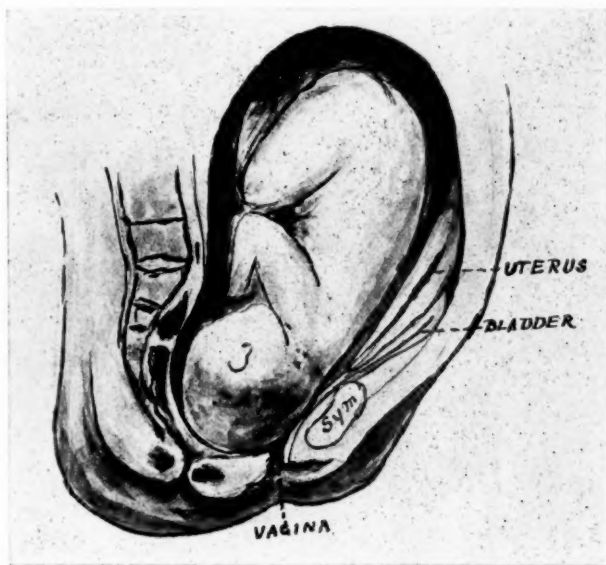


Fig. 1.—Shows the head well in the pelvis pressing down on the pelvic floor. Uterus enlarged and flattened out in front.

gestation, she came to the hospital prenatal clinic where her general condition was so satisfactory that at first extrauterine pregnancy was not recognized. April 8, the last time she visited the clinic, she was found to be in the last month of gestation. The abdomen was pyriform in shape. The abdominal wall was thick and tense and it was difficult to outline the fetal ovoid but the fetal heart could be easily heard to the left and below the umbilicus. Above the pubic symphysis and pushed to the left side was found a more resistant mass which proved later to be the uterus flattened out and the size of a three months' pregnancy. Rectal examination revealed the head well engaged in the pelvis and to the level of the ischial spines. It was not until later when a vaginal examination was made that the diagnosis of extrauterine pregnancy was confirmed. In studying the position of the head, it was found that while it was in the pelvis, it was not in the uterus nor was it in the vagina. A thin membrane between the examining finger and the head was found to be the septum between the vagina and Douglas' pouch stretched to an almost incredible thinness. (Fig. 1.) The cervix could not

at first be found for the well-developed head had lifted the uterus completely out of the pelvis and only with great difficulty was the cervix finally reached high up above the symphysis to the left side. (Fig. 2.) So thin was the septum between the head and the vaginal wall and so difficult was it to find the cervix that it is conceivable that the same might have been mistaken for the fetal membranes, possibly punctured and an attempt made at delivery through the vagina. Upon admission to the hospital April 25, she complained of slight pains throughout the abdomen and bladder irritability. These symptoms had developed that morning. Her pulse and temperature were normal and the fetal heart easily heard. As her condition was so satisfactory, it was decided to operate the following morning.

Operation: An incision, 16 cm. in length, was made to the right of the median line. Free fluid was found in the abdominal cavity and a small rent in the gestation sac was discovered. The uterus, about the size of a three months' pregnancy



Fig. 2.—The uterus in front of the head and lifted out of the pelvis.

was found in front of the fetal sac and displaced to the left side by the presenting part. The left oviduct was normal. The dorsal plane of the child was on the left side and the head well in the pelvis as in a normal uterine pregnancy (first position of the vertex). It was now found that the omentum covered a large portion of the fetal sac. In enlarging the rent above mentioned to deliver the child, there was profuse bleeding caused by separation of that portion of the placenta which was attached to the posterior surface of the omentum. The child was rapidly delivered, was in no way deformed and soon began to cry. Although of normal size in frame, it was poorly nourished weighing 2850 gm. (5 pounds, 15 ounces). The pregnancy had its origin primarily, in the right tube, probably tubal abortion as no injury to that organ was discovered. The placenta, which was annular in shape, was attached to the tube, the posterior surface of the right broad ligament and omentum. It was prevented from encroaching upon the cavity of the true pelvis by the growing fetal head. It received its blood supply from

the omental vessels and branches of the ovarian and uterine arteries. When the child was delivered and the sac freed of blood, it was decided that the placenta could be removed without too great a risk of hemorrhage. This was carried out first by removing a large portion of the omentum, then by ligating the ovarian and uterine arteries. With this control of the blood supply, the placenta could be peeled out easily with very little bleeding. As it was impossible to remove the entire sac, particularly that portion occupying the pelvic cavity and as there was some oozing of blood, a small abdominal drainage tube of soft rubber was placed in Douglas' pouch and fixed at the lower end of the incision. The patient was returned to her bed with a pulse of 120 and given 500 c.c. of a 10 per cent glucose solution intravenously. On the ninth day postoperative, she passed a foul-smelling mass from the vagina which on pathologic study proved to be a decidua cast of the uterus. On the twelfth day although her general condition seemed to be satisfactory, a blood count showed 1,910,000 erythrocytes, 31,950 leucocytes, and the hemoglobin 37 per cent. She was given a blood transfusion of 575 c.c. This was followed by an immediate increase in the red count to 3,000,000 and an increase in the hemoglobin to 50 per cent. From this time on the patient's convalescence was satisfactory and May 28, 1929, thirty-two days after the operation, she was discharged in good condition, the child having gained over one pound. Nine months later the baby weighed 16 pounds. Both are in good health.

These cases are interesting from several standpoints. It was surprising how little discomfort these patients had until the end of gestation. The first case should have been operated upon at an earlier date when the child was alive and could have been saved. It occurred thirty-four years ago and the delay in operating was probably prompted by the thought that after the death of the child and placental separation had taken place, the mother's life would be safeguarded.

We were fortunate in the second case in finding it possible to immediately remove the placenta. As the patient was not infected, the abdominal drainage tube might have been omitted.

DISCUSSION

DR. EDWARD A. SCHUMANN said the most interesting problem connected with these cases lies in the position of the placenta. He still felt doubtful, however, about leaving so large a mass of tissue in the abdomen, for fear of infection. Within the past three years he has so left the placenta, cutting the cord close to it. Careful bimanual examination some eighteen months after the operation failed to reveal any evidence of foreign tissue in the abdomen.

DR. BARTON C. HIRST felt there was a very serious risk of separation of the placenta, and fatal hemorrhage can ensue within a few hours after closure of the abdominal cavity.

DR. NEWLIN F. PAXSON said that he had a case at Hahnemann Hospital of a girl whose last menstrual period was in November, and who had an abdominal abortion in December. She came into the hospital in June, about five or six months' pregnant. There was some doubt as to whether she might have had a secondary abdominal pregnancy.

The baby died in the thirty-first week of pregnancy. She was operated upon a week later, the baby removed and the placenta separated. After a stormy convalescence she eventually recovered, after passing a large mass of placenta through the abdominal wound.

DR. BOYD (closing).—It was surprising to find in both cases so little discomfort up until the onset of spurious labor, and it is usually justifiable in the interest of the child to let the pregnancy advance to the thirty-eighth week of gestation.

Diagnosis would seem to be comparatively easy in such cases but is often confounded with fibroid of the uterus and cornual pregnancy. In my second case the fetus was in a normal position and the head well into the pelvis. It was the high position of the cervix above the pelvic brim that directed our attention to extrauterine pregnancy.

DR. MAX TRUMPER (by invitation) presented a paper entitled **Fundamental Biochemical Factors in Pregnancy**. (For original article see page 209.)

DISCUSSION

DR. J. STUART LAWRENCE agreed with Titus that there is a relative and also an absolute hypoglycemia in eclampsia, which Dr. Laferty, of Philadelphia, had been able to confirm by following closely Titus' technic. Failure to read the blood at frequent intervals may be one cause of the differences in the findings of Stander from those of Titus. However another feature was that even in their routine clinic examinations they, Lawrence and Laferty, always found a hypoglycemia in the severe stage of the hepatic type of toxemia and of eclampsia.

DR. DANIEL LONGAKER said that he has tested out calcium gluconate intravenously. The results of its use are very marked, almost spectacular. The benefits, especially in early toxemia of pregnancy, are prompt and pronounced, and the same is true in the later period.

However, in private practice there is comparatively little opportunity to see the ultimate results of toxemia; it has become rare for a private patient to develop eclampsia.

Calcium gluconate he believed filled definite indications and produced beneficial results throughout the entire period of pregnancy. This conviction was based on a large number of observations recently made.

DR. TRUMPER (closing) said that in the face of such positive findings with regard to both hypoglycemia and hyperglycemia in eclampsia, some attempt should be made to reconcile the opposing views of the two schools of investigators. In connection with studies of this nature the condition of carbohydrate stores in the body must always be taken into consideration. This fact has been recognized by most observers but difficulties arise in the study of patients with eclampsia because of the practical impossibility of adequately controlling the nutrition of these individuals for the several days prior to their admission to hospitals in active eclamptic states. It is a known physiologic fact that in the presence of an adequate glycogen reserve in the liver certain factors such as severe exercise, convulsive seizures, acidosis, severe emotion, and certain toxic states may result in hyperglycemia due to increased hepatic glycogenolysis. Any factor which produces hyperglycemia by increasing glycogenolysis in the liver will eventually produce hypoglycemia if the glycogen reserve of the liver is not restored. Therefore it may be understood how the blood sugar findings in a condition such as eclampsia may show marked variations depending upon the supply of glycogen in the liver at the time the patient is first seen and upon the ease with which this glycogen reserve may be maintained during the course of the disease.

Dr. Longaker's mention of the satisfactory results obtained by the use of calcium gluconate in the early toxemias of pregnancy is in accord with the results obtained by Minot and Cutler previously mentioned.

DR. LEONARD AVERETT read a paper on the **Advantages of Kerr Cervical Cesarean Section**, in which he described his personal experience with this procedure in a series of eighteen cases, six of which were doubtful as to possible infection.

In the clean cases are included only those in which all examinations were made in the hospital. Of these, 6 were elective cesarean sections. Six had a test of labor varying from six to twenty hours and all examinations were made per rectum. In 3 cases the membranes had been ruptured from four to eighteen hours before operation.

Of the six doubtful cases two patients had unsuccessful application of forceps, one at home and one at the hospital. One case was a transverse position with a prolapsed hand in an old primipara with a moderately contracted pelvis. The membranes had been ruptured for nine hours, and numerous vaginal examinations were made in the patient's home by the family physician.

Another patient with a contracted pelvis was in labor for twenty-eight hours at home, membranes ruptured for sixteen hours, and had a temperature of 101° F. upon admission to the hospital. An ovarian cyst prolapsed into the culdesac made operative interference necessary. While the patient was in labor at home for many hours repeated vaginal examinations were made. A large baby in a forty-two year old primipara with a rigid cervix in labor at home for 24 hours was another one of this series. The operations were performed under spinal anesthesia in most of the cases. The convalescence in the elective cases was very smooth and in some, differed very little from a convalescence in a normal spontaneous delivery.

DISCUSSION

DR. JOHN A. McGLINN said that he did not see any particular benefit in this operation because there was so much danger of extension of the longitudinal incision. Certainly in any case of low cervical operation, whether it is a transverse or a longitudinal incision, hemorrhage is bound to occur.

There is no doubt at all, he added, that spinal anesthesia greatly facilitates the operation. He anesthetized all his patients in the upright position because he does not use the Pitkin technic. His patients have been entirely free from headache.

Dr. McGlinn said that they have also added music to the operating room routine, where patients are being done under a spinal anesthetic, and that he had found it a great advantage. He said his experience was that the music not only helps the patients, but also the workers in the theater. He said it acted as a shock absorber, and that though it might sound trivial, he had found it to be of definite psychologic benefit.

DR. EDWARD A. SCHUMANN said that the most alarming hemorrhage he had seen was in a case done under a local anesthetic. He said he had had two accidents: one where the lower uterine segment had not been sufficiently distended, with furious hemorrhage; the other was the case of a woman who had been in labor many hours and the lower uterine segment had been so thinned out that hemorrhage was inevitable. In both cases, however, the bleeding was controlled.

DR. AVERETT (closing) said that he found no disadvantage in doing this operation in elective cesarean sections where there has been no test of labor and the lower uterine segment has not been thinned out, the reason being that the space required for the incision is in the transverse and not in the longitudinal diameter.

As to the danger of cutting into the uterine arteries, this can be obviated by making a curved incision with the convexity toward the bladder, thereby avoiding injury to the uterine vessel.

In the case referred to by Dr. Hirst, he found unusually large veins running across the lower uterine segment. Had the transverse incision been made he would have cut across these veins and produced severe bleeding. With the possibility of such a complication in mind, he used the longitudinal incision and had no abnormal amount of bleeding.

Spinal anesthesia was used and crystals of novocain were dissolved in the spinal fluid. This was given with the patient sitting up and immediately after the injection the patient was placed in the Trendelenburg position. He had used this form of anesthesia in three to four hundred cases for gynecologic and upper abdominal operations. The results have been up to the present time uniformly good and without complications such as paralysis, headaches, etc.

DR. DANIEL LONGAKER said that he felt, that Dr. Averett had departed from one fundamental point in the technic of spinal anesthesia as advocated by Pitkin, and that was in not making the injection with the patient in the recumbent position, the head lowered.

He said that he and his colleague, in some twelve recent sections, invariably placed the patient in the horizontal position, with the head slightly lower than the body. Both he and Dr. Harriman felt convinced there was an added element of safety in this precaution, although it is frequently more difficult to enter the spinal canal when the patient is lying down.

While the previous speaker (Dr. Hirst) was uttering his word of warning, Dr. Longaker said it occurred to him to ask whether his work is done under a general anesthetic or under spinal anesthesia. The absolute relaxation of the abdominal muscles is one of the most important facts noticed in operating under spinal anesthesia, and it makes the low transverse cervical cesarean comparatively easy. Moreover the absence of gas pains, vomiting and distension, as well as the fact that one can give orange juice and fluids almost immediately afterwards is a distinct advantage.

The low transverse cervical cesarean section under spinal anesthesia is satisfactory and the operation relatively safe, especially in toxic cases where there is a certain degree of hypertension, elevation of blood pressure, and comparative bloodlessness of the field.

According to his experience one need not wait for the lower zone to thin out before doing the Kerr operation.

DR. BARTON C. HIRST said he saw this operation performed in Glasgow in 1926, before it was published and he had done the first one in Philadelphia. He felt it was a good operation under certain circumstances, but that it should not be used routinely, because he thought there were more cases of hemorrhage in this method than in any other, very alarming hemorrhage, sometimes. It was essential that the operator should always be provided with instruments that would control such hemorrhage. It is not, he said, an operation which should be performed before labor has begun.

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF MARCH 7, 1930

DR. BRUCE HARRIS reported a case of **Tuberculosis of the Cervix**. (For original article see page 249.)

DISCUSSION

DR. GORDON GIBSON.—I want to confess that when this patient came into the service I did not know she had tuberculosis, and I think if I saw another case just like it I would not know she had it.

However, there is one thing in this case that we should have thought of. This woman did not look very well; she was rather below par, and did have evidence of an old pulmonary lesion.

DR. SAMUEL A. WOLFE.—In reporting on this slide which was sent to the laboratory, the question arose as to whether we were dealing, in the first place, with tuberculosis or with another type of granuloma, possibly chancre, and the second question that arose was: Is this primary tuberculosis in the cervix or secondary to the more usual tuberculosis of the tubes? From the pathologic standpoint, we feel justified in excluding syphilitic infection for the following reasons:

In the first place, the multiplicity of the lesions; that is, in chancre there is a solitary lesion. In this particular cervix there were multiple foci of granulomas. The granuloma itself was different, being comprised of large epithelioid cells and, as the slides very well show, giant cells. The plasma cell, which is so frequent in chancre, and the perivascular infiltration, which is commonly found in chancre, was missing in this particular slide; so, without subjecting the tissue to specific stain by the Levaditi method, we, nevertheless, felt certain that we were dealing with a tuberculous granuloma and not a chancre.

The unusual point in this case is the primary site in the cervix.

Incidentally, in the last six years I have encountered but four cases of tuberculosis of the uterus; three were instances of tuberculous endometritis and metritis secondary to tuberculosis of the tubes. This is the only instance of seemingly primary tuberculosis of the cervix. After the hysterectomy was performed in this case we made a very careful and painstaking search, making multiple sections through the tubes, ovaries, and body of the uterus to exclude tuberculosis higher in the pelvic viscera. This, I feel, has been satisfactorily excluded, and I think this case may be authentically recorded in the literature as a primary instance of tuberculosis of the cervix.

DR. JAMES W. DUNCAN, MONTREAL, QUE., read a paper (by invitation) entitled **The "Radical" in Obstetrics**. (For original article see page 225.) The discussion was participated in by Drs. Humpstone, Bishop and Kosmak.

DR. HENRY B. BOLEY reported a case of **Purpura Hemorrhagica Complicating the Puerperium**. (For original article see page 252.)

Correspondence

To the Editor.—For the past year I have employed a satisfactory and what I believe to be a new procedure for assisting the completion of the third stage of labor in a physiologic manner.

I wish to present a description of this method as well as my reasons for adopting it.

Normally the placenta separates from its uterine attachment during the pain or uterine contraction completing the second stage of labor. If the delivery of the baby is completed without a pain as by forceps or extraction, then the first after-pain influences the separation of the placenta from its attachment.

Langhans in 1875 showed that a well-developed zona spongiosa is a necessary foundation for a normal placental separation. With a diminution or absence of the spongy layer, a pathologic anchoring of the villi in the uterine musculature begins. This has been shown in many cases reported in the literature.

With the firm contraction of the uterus, as the fetus is expelled, the following occurs: the muscular wall of the uterus becomes thick and hard, the compact layer of the placenta is squeezed free of blood (that in the fetal vessels enters the body of the baby while the blood in the maternal sinuses of the placenta empties into the zona spongiosa). This spongy layer, distended with blood is compressed as in a vise, between the hard contracted uterine muscle and the firm compacta of the placenta, causing rupture of the fine fibrillae of the spongiosa. The placenta therefore separates completely and not in parts. Where the placenta is very thin and extensive this does not take place, and it is frequently found that such placenta remains adherent to the uterine wall.

I do not believe as is generally assumed that placental separation takes place as the result of a retroplacental hematoma although bleeding occurs and accumulates behind the separated placenta. As the maternal surface of the now separated placenta cannot accommodate itself to the diminished uterine surface the placenta folds or "doubles" on itself and lies just above the contraction ring. It is not expelled from the upper contracting part of the uterus as yet because it is held by the firm adhesion of the membranes around the placental border. The uterus has now accomplished all that its muscular contraction, acting on the placenta alone, can do. With the formation of a retroplacental hematoma, further contractions of the uterus acting on this clotted blood as a driving wedge, force the separated placenta downward into the lower uterine segment, peeling the membranes off the uterine wall. As this hydraulic action continues the placenta is expelled into the vagina. If this mechanism fails as is evidenced by external bleeding from the placental site coming from between membranes and uterine wall, there is delay in the downward passage of the placenta.

Manipulation of the uterus during the third stage frequently interferes with this normal mechanism.

To aid in the conduct of this period of labor, I have managed my cases as follows: Following the birth of the child, the "hands off" dictum of Ahlfeld is strictly adhered to. The baby is attended and the cord is cut, cord dressing applied and the perineum inspected. These procedures are done slowly so that five minutes are allowed to elapse following the birth of the baby before any further interference is practiced. Of course, during this time one observes the size of the uterus, the amount of blood lost and the appearance and pulse of the patient. An

Ochsner forceps is now placed transversely on the cord close to the vulva. Holding this clamp in one hand, the other hand is placed on the abdomen above the symphysis. (The radial border of the hand is directed toward the mother's spine while the palmar surface is directed upward toward the diaphragm.) The body of the uterus now lies in the palm of the hand.

Intermittent pressure is made upward on the body of the uterus still holding the clamp at the vulva. As these "pushes" on the uterus are made, the uterus rises higher and higher in the abdomen and the placenta glides into the lower segment and upper vagina. As this is occurring one feels (with the abdominally placed hand) the peeling of the membranes from the uterine wall. The "pushes" must be made with gentleness. If the contraction ring is firm or the placenta has not separated, then the upward push on the uterus will pull upward on the clamp in the other hand. When this occurs no further attempts should be made for five minutes when the maneuver is again repeated. There must be no traction on the cord but it must be held taut.

When the uterus is high up in the abdomen, the assistant or nurse places her hand in the same position on the abdomen holding the uterus high. Gentle downward pressure above the symphysis now expels the placenta from the vagina.

The uterus is held up for fifteen minutes as a prophylactic measure against the occurrence of hemorrhage.

I have conducted two hundred labors in the above manner and have found that there is very little blood lost during the third stage. The retroplacental hematoma is usually absent or may be small in volume.

The upward held uterus contracts firmly because the uterine muscle is anemic, due to the tension on the uterine vessels. There has been no severe loss of blood in any of these cases.

This maneuver is of great value in the treatment of postpartum hemorrhage due to atony of the uterus. The bleeding can be almost instantly controlled by pushing the uterus upward out of the pelvis almost into midabdomen. The tension on the uterine vessels and the avoidance of passive congestion that is usually produced by the Credé maneuver or downward pressure, allow the atonic uterus to regain its tone and contract. This procedure alone may suffice to control the hemorrhage but other measures should also be used.

In patients delivered under deep anesthesia by forceps or extraction, one must wait for the first after-pain to effect separation of the placenta before performing this mode of delivery. This usually takes from ten to fifteen minutes. The success of the procedure depends upon the placenta being separated; hence it must fail in placenta accreta and adherent placenta.

There have been no untoward results from the use of this plan of treatment.

I desire to place my observations on record and intend at a later time to present a more detailed account of the procedure and a more thorough discussion of the physiology involved.

MURRAY L. BRANDT, M.D.

2021 GRAND CONCOURSE, NEW YORK.

American Journal of Obstetrics and Gynecology

GEORGE W. KOSMAK, M.D., EDITOR

HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Editorial Comments

Protection Against Possible Abuse of the Aschheim-Zondek Pregnancy Test

PATIENTS and physicians readily appreciate one feature of the Aschheim-Zondek test, namely, that it belongs to that unfortunately small group of tests which in their execution inflict upon the patient not the slightest pain, discomfort, or even inconvenience. All she has to do is to send a specimen of morning urine to the laboratory. And now we are told by Stern in a recent number of the *Zentralblatt fuer Gynaekologie* that this very feature of the test renders it particularly useful for spying, deception, fraud, and other like procedures practiced with dishonest intent. Some one might surreptitiously get hold of such a tale-telling bit of urine and find out many things he ought not to know. A suspicious husband could secure proof positive of the faithlessness of his wife. Parents could keep careful watch over the daughter leading the gay life of the day. The lady of the house, insisting upon perfect morality, could keep track of the doings of her servants. How simple for the roommate to find out whether her girl friend is in trouble. The young man of town could keep track of his lady love—to break quickly with her in case the outcome of the test would not be to his liking. The cunning and informed sweetheart could procure some urine from a less fortunate girl friend and thus hasten a marriage of which she feels not any too certain. And the other way around, substitution of urine from a nonpregnant woman would be an easy means of dissimulating an existing pregnancy, and then quickly another lover could be procured financially better equipped to pay alimony.

These examples of possible abuse might suffice, and with satisfaction we acknowledge that Stern has not so far met with any of them in reality. With the same systematic thoroughness he elaborates the

measures required for full protection against such possible deception: (1) Urine must be obtained directly from the patient only by means of catheterization; (2) the test should be made only by physicians; (3) the test is made only when demanded by the patient; (4) the result of the test is communicated only to the patient.

We beg to assert that even these precautions would still leave ample opportunity for deceiving husband or lover on the basis of the Aschheim-Zondek test.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Selected Abstracts

Carcinoma

Kanki, Y.: **Statistics of Uterine Cancer.** Japanese J. Obst. & Gynec. 12: 12, 1929.

The author could not prove any relationship between the number of labors and cancer of the cervix uteri. The latter was found to be most frequent between the ages of thirty and sixty and the average age was forty-four and one-half years. The spindle cell type was found among the younger women whereas the fat spindle cell type was prevalent among the older ones. The spindle cell type frequently attacked the lymphatic glands but only rarely affected the connective tissue (parametrium). On the other hand, the fat spindle cell type acted in the reverse way. Recurrences were more frequent with the spindle cell type.

J. P. GREENHILL.

Hoffman, F. L.: **Cancer in Hawaii.** Address delivered before the Pan-Pacific Surgical Congress, Honolulu, Aug. 17, 1929.

Cancer in Hawaii during the last five years has shown no pronounced tendency to increase. The cancer death rate in Hawaii is measurably below the average for most other civilized countries or localities. The most important form of cancer is that of the stomach and liver. Cancer of the female genital organs and the breast appears not to be excessively common among any of the various racial elements. There was no cancer of the breast among Japanese women which is in strict conformity with the rarity of this form of disease in Japan. Among the women in the Hawaiian Islands the outstanding form of cancer is that of the uterus, there having been 128 deaths from this form of the disease out of a total of 364. Cancer of the breast caused only 22 deaths out of the 364 deaths.

J. P. GREENHILL.

Horwitz, Alec: **Incidence of Carcinoma of the Uterus Among Jewish Women.** Surg. Gynec. Obst. 44: 355, 1927.

Racial immunity to carcinoma, the ritual dietary laws, poverty, and the more normal blood supply to the generative organs in Jewish women, have been some of the reasons advanced to explain the relative infrequency of carcinoma of the uterus in Jewish women. These, and many other reasons, however, have been refuted by other authorities; the fact still remains that in spite of the fertility and longevity of Jewish women, carcinoma of the uterus is relatively infrequent among them.

Of 1,237 cases of primary carcinoma of the uterus seen at the Mayo clinic between 1920 and 1925, inclusive, 1,227 were among gentiles and 10 were among Jewesses. Ninety-seven per cent of the 1,237 patients were married.

From data obtained at the Curie Hospital, where two-thirds of the patients were treated for carcinoma by roentgen rays or radium, the incidence of carcinoma was slightly less for the Jewish patients (62 per cent) as compared with carcinoma in the gentiles (66 per cent).

Carcinoma of the uterus is comparatively infrequent among Jewesses, being about one-fourth as frequent as in the gentile women (3.9 per cent as compared with 16.5 per cent).

Carcinoma of the breast in the female is common among Jewesses and almost equals the percentage in gentile women, the incidence being 26.4 per cent and 28.3 per cent, respectively.

Carcinoma of the digestive tract, including the liver and pancreas, was almost twice as frequent in the Jew as in the gentile, being 30.2 per cent and 17.1 per cent, respectively.

WM. C. HENSKE.

Wistein, R.: The Cancer Problem. Med. Woman's J. 26: 201, 1929.

This is a review of the literature on cancer, including theories as to etiology, diagnosis, and treatment. Under the latter head the author takes up in detail treatment with emetin hydrochloride, stating: (1) Emetin will cure early carcinoma. (2) It will prevent the return in operable cases if used in connection with surgical treatment. (3) It will widen the field for operable cases by making inoperable, operable. (4) It will relieve the pain and odor in the last stages of advanced cases.

FRANK SPIELMAN.

Schiffman, J.: Causes and Treatment of Postclimacteric Bleeding. Wien. klin. Wchnschr. 42: 53, 1929.

In discussing the causes of postmenopausal bleeding the author includes "kolpodystrophia postclimacterica desquamativa" (which he believes is a better term than "kolpitis vetullarum"), vaginal carcinoma, cervical and fundal polyps, and carcinoma of portio, uterus and ovaries. He emphasizes that in cases where no cause for bleeding can be found in spite of curettage, an ovarian carcinoma, which may produce only transient bleeding, be looked for.

In treatment he prefers operation plus x-ray for carcinoma of both cervix and fundus whenever possible. He deplors the tendency to perform hysterectomy without diagnostic curettage where no cause for bleeding is found, and advises that if operation in these cases is decided upon, the adnexa also be extirpated. In cases where careful study has produced no evidence of abnormality, he recommends observation especially for the presence of ovarian carcinoma.

FRANK SPIELMAN.

Oki, Tsunemtsu: On the Relation of Glycogen and Carcinoma of Cervix of Uterus. Japan Med. World 7: 108, 1927.

The author has analyzed the cases coming to the gynecologic clinic at Aichi Medical College from August, 1922, to May, 1927. His classification of cervical tumors with percentage of each is as follows:

1. Primary solid carcinoma - - - - - 95 per cent (Total)
 - (a) Ripe carcinoma - - - - - 7.4 per cent
 - (b) Medium ripe carcinoma - - - - - 52.6 per cent
 - (c) Unripe carcinoma - - - - - 40.0 per cent
2. Primary glandular carcinoma - - - 5 per cent (Total)
 - (a) Glandular carcinoma - - - - - 60 per cent
 - (b) Malignant adenoma - - - - - 40 per cent
3. Mixed form.

Glycogen was found in 60.6 per cent of the solid carcinoma and in 20 per cent of the glandular type. Glycogen was also found in the leucocytes about the tumors. The author quotes the statistics of numerous other writers, some maintaining that the glycogen appears in cells that are growing and others claiming that the substance is found only in cells that are losing metabolic activity. The author shows that in his cases he has found that it appears in cells which are losing their metabolic activity or have no activity and yet are not atrophic. He has noticed an increase in glycogen in tumors treated with radium. He concludes that glycogen is due to a disturbance of sugar metabolism caused not only by circulatory disturbances but also by physiochemical influence (as radium).

GENE M. KASPER.

Lahm: The Glycogen Content of Uterine Cancer. *Ztschr. f. Geburtsh. u. Gynäk.* 93: 356, 1928.

Glycogen has been found in carcinomas of the skin and mucous membranes but not in those of the breast, large intestine, ovary, and most adenomas. It is demonstrated in the cells of the tumor by using Best's stain.

The author investigated 20 cases of cancer of the cervix, one of the fundus, and four normal cervixes by staining sections for glycogen.

Thirteen cases of cancer of the cervix were of the ripe type, i.e., differentiated, and eleven of these contained glycogen in large amount. Those which were unripe contained little or none. The sections showing normal epithelium contained glycogen when the cells were well differentiated but where they were growing over an erosion and were therefore young, less ripe cells, glycogen was not found.

The squamous epithelium of the vagina and cervix of the mature female always contains glycogen. It is not known whether this changes with the menopause. It is certain that the amount of glycogen decreases when the change to carcinoma occurs. There may be some relation to the ovarian hormone but a case examined before and after ablation of the ovaries has not been obtained.

Adenocarcinoma of the fundus and cervix does not contain glycogen unless epithelial pearls are formed and these do contain it.

This study may help in the diagnosis between precancerous and true carcinoma of the cervix.

FRANK A. PEMBERTON.

Guthman, H., and Hess, L.: Antitryptic Index In Carcinoma. *Arch. f. Gynäk.* 131: 463, 1928.

The antitryptic content of the blood serum in carcinomatous patients varies but averages higher than in normal healthy patients. Immediately following radiation therapy there is a definite increase in this antitryptic index. This gradually returns to its former normal value. The authors conclude that the test has no prognostic value.

RALPH A. REIS.

Novak, Emil: The Recognition of Early Cervical Cancer. *Surg. Gynec. Obst.* 50: 200, 1930.

The early diagnosis is often difficult, but it means much to the patient, as it gives her a relatively good chance for life. It requires experience, a careful pelvic examination, including the use of the speculum in a good light and in a certain proportion of cases, biopsy and microscopic examination. Biopsy is indicated if there is an indurated area on either cervical lip, especially if the overlying surface is granular, vegetative, or ulcerated and very vascular. It is also indicated if in an erosion or

ectropion there is a hardened or raised area, with vascularity, sponginess, or tendency to ulceration of the surface.

Biopsy may be performed with a sharp knife or punch followed by searing of the wound edges with the cautery. The tissue should be excised from the most suspicious area, and the sections should be cut in such a manner as to show the mucous surface. It is desirable to cut a number of sections at different levels in the block.

The pathologic examination should be made by a competent pathologist, preferably by one thoroughly familiar with the special pictures encountered in this field. In a small residuum of cases the diagnosis may be impossible. In such cases the proper procedure is to wait for a few weeks and then repeat the procedure.

The great majority of cervical lesions is obviously benign so that biopsy and microscopic differentiation need be invoked in only a small proportion. If the pars vaginalis is normal in appearance but the intracervical mucosa seems vascular or granular, the curette may reveal definite intracervical cancer, most often adenocarcinoma.

If, as is most often the case, the suspicious lesion is found to be benign, it should be eradicated by whatever method is best suited to the individual case. Usually some simple procedure often of the office type is sufficient. These lesions unquestionably predispose to cancer, when combined with the still unknown factor of individual susceptibility. Their eradication is the one important contribution we can make to the direct prophylaxis of cervical cancer.

WM. C. HENSKE.

Victor-Pauchet: A Danger of Biopsy in Cancer of the Fundus: Uterine Perforation. Bull. et mém. Soc. des chir. de Paris 14: 726, 1928.

The author reports the case of a woman sixty years of age in which the fundus was perforated during a diagnostic curettage. The perforation healed spontaneously. One year later the patient consulted the author because of pain in the abdomen. Laparotomy showed a somewhat enlarged uterus on the superior surface of which was a newgrowth. A loop of intestine had been surrounded by the newgrowth. A complete hysterectomy and resection of the adherent bowel were carried out. Six months later the patient presented a metastasis of the large omentum in the region of the epigastrium. Gross and histologic diagnosis was cancer of the uterine fundus.

In discussing the case Victor-Pauchet points out that in suspicious cases of uterine bleeding where the cervix is negative the fundus should be suspected. In these cases he is opposed to biopsy relying on the clinical manifestations for a diagnosis. Biopsy by curettage is dangerous both because of the danger of perforation and because cases have been reported where a negative biopsy report was followed in one to two years by death from fundal malignancy. Therefore in all cases of bleeding in patients past the menopause and in which the cervix is negative, a hysterectomy, either abdominal or vaginal, should be immediately resorted to. Should an infected or cancerous uterus be perforated by curettage a hysterectomy should be done immediately; on the other hand perforation of a benign uterus is not dangerous.

THEODORE W. ADAMS.

Léo: Biopsy in Cancer of the Fundus. Bull. et mém. Soc. des chir. de Paris 15: 768, 1928.

Léo agrees with Victor-Pauchet that when the clinical symptoms of fundal carcinoma are sufficiently clear, a hysterectomy should be done without diagnostic curettage. On the other hand he stresses that fragments of all curettages should be sent to the pathologist for a microscopic examination. Care should be used in doing a curettage so that the entire uterine cavity is thoroughly covered.

THEODORE W. ADAMS.

Bailey, K. V.: An Inquiry Into the Basic Cause and Nature of Cervical Cancer. Surg. Gynec. Obst. 50: 513, 1930.

The various aspects of erosion in all its phases and degrees, its associated cellular activities, and its histologic eccentricities are thoroughly described in this paper. The ultimate sequel to erosion is malignancy, but there is the phase between these two which must be bridged, the premalignant phase which must contain the primary malignant reactions. This study has aimed at the recognition beyond doubt of these earliest manifestations of cancerous change, in the hope that some light may thereby be thrown upon the origin of this disease.

WM. C. HENSKE.

Graves: Relationship of Imperfect Drainage to Genital Cancer in the Female. Am. J. Surg. 3: 489, 1927.

Graves cites five cases of cancer occurring in women who had atresia somewhere along the genital tract. He claims the retained secretions are a causative factor because of their irritating effect. The advisability of exercising more care to avoid stricture in plastic operations and a closer observation of the postclimacteric patient is emphasized by Graves.

WILLIAM KERWIN.

Blind, Auguste: Mucous Polyps and Uterine Cancer. Bruxelles Med. 10: 322, 1928.

The author reports two cases of polyps of the cervix which on microscopic examination were shown to be of the simple mucosal variety. In both cases the patients, a few months later, developed carcinoma of the fundus. He, therefore, feels that the appearance of simple polyps in women past the menopause probably is secondary to other pelvic pathology and should suggest a possible malignancy of the uterus.

THEODORE W. ADAMS.

Condamin, R.: Cancer of the Cervix in a Pregnant Uterus. Gynec. 27: 577, 1928.

The author reports 4 cases of cancer of the cervix complicating pregnancy. He believes that a pregnant uterus tolerates very well the usual dose of radium but it is advisable to keep the patient under the influence of morphine in order to help this tolerance. In two of the author's cases, labor took place through the natural passages, but these cases are exceptional and require careful watching. The usual method of delivery should be by cesarean section. The author maintains that the fetus is not affected by radium even if applied in the early weeks of gestation. He believes that when radium is applied in the sixth or seventh month, it is best to perform a hysterectomy after the child is delivered. On the other hand, when radium is administered early and repeatedly, another application after delivery is preferable. Treatment should be instituted early in every case without considering it dangerous for the child.

J. P. GREENHILL.

Miller: Prophylaxis of Cancer with Special Reference to the Cervix Uteri. New Orleans M. & S. J. 80: 253, 1928.

Schereschewsky, in the United States Public Health reports for 1926, states that one patient dies of cancer every four minutes, and that between the ages of forty-five and sixty-five, one out of every five women succumbs to this disease. For this reason Miller feels that too much cannot be said as to the prevention of cancer. By far the majority of cancers in women originate in the cervix uteri. This organ is

readily accessible to examination, and the forerunners of cervical malignancy (laceration or eroded cervix) may therefore be found and corrected. A vaginal discharge is not a normal condition and cases with this manifestation should be subjected to thorough examination with biopsy and microscopic examination of the removed tissue. In this way alone can uterine malignancy be discovered in the curable stage. It is the responsibility of the medical profession not only to conduct such examinations but to disseminate the knowledge of their necessity among the laity.

THEODORE W. ADAMS.

Jeanneney, G.: Cancer of the Cervical Stump After Subtotal Hysterectomy.
Rev. franç. de gynéc. et d'obst. 24: 273, 1929.

The author emphasizes that every cancer found in a cervix after subtotal hysterectomy does not constitute a case of cancer of the cervical stump. In many cases cancer or latent cancer was present at the time the body of the uterus was removed. An interval of time, preferably at least a year or two, should elapse between the operation and the finding of cancer in the cervical stump to make a case authentic. At the cancer center of Bordeaux and the South West among approximately 1800 cancers of the cervix seen from 1925 to 1929 there were nine cancers of the cervical stump. The author believes that this type of cancer is no more frequent than cancer of the cervix in women not operated upon, hence subtotal hysterectomy does not predispose the cervix to cancer.

In 90 per cent of the cases reported in the literature the body of the uterus had been removed because of fibroids. The incidence of this type of cancer decreases as the length of time the operations was performed increases. The prognosis of this type of malignancy is very grave. The literature indicates that more than 50 per cent of the patients died in spite of operation and radiation therapy. The only prophylaxis is to perform a total hysterectomy routinely but this is not necessary except in simple cases in which there are cervical lesions, in syphilitic patients and in those with fibroids. In all other cases, a subtotal hysterectomy is sufficient.

The treatment of cancer of the cervical stump in early cases is by abdominal operation, for by this means, not only may the cervix be removed but also the broad ligaments. When resection is attempted vaginally, there is difficulty in removing the entire cervix because it is friable. Great care must be exercised in applying radium in the cervical canal because of the possible proximity of intestinal loops. The safest thing to do is to systematically examine all patients who have had operations and to institute treatment as soon as any sign of cancer is observed.

J. P. GREENHILL.

Lovegren: Carcinoma of the Vagina in Second Year of Life. *Trans. Finnish Med. Soc.* 71: 717, 1929.

The writer records a vaginal carcinoma in a girl seventeen months old, representing an extremely rare observation. A drop of blood appearing in voided urine of a seemingly healthy infant furnished the first symptom.

When first seen child was well nourished, urinary findings negative. Through an ear speculum introduced into vagina a dark red, irregular thickening was seen on the right posterior wall covered by a dirty looking membrane. A tumor in vaginal wall was palpated through rectum, the uterus lying clearly separated from it. Microscopic study of tissue removed revealed a malignant, papillary, epithelial mass.

Disease progressed rapidly. Cachexia, loss of weight, anemia and fever soon appeared. Radical surgery was refused by the parents, and application of radium resulted in temporary remission of symptoms. Tumor increased, foul, bloody discharge and metastases developed in abdominal wall and right lumbar region. Death occurred six months after first symptoms.

REUBEN L. LARSEN.

Pettit, R. T.: Intravenous Lead in Treatment of Cancer. Illinois M. J. 55: 9, 1929.

The use of intravenous lead in treatment of cancer is founded on a very substantial theoretical basis which is now supported by a mass of scientific data worked out by the Liverpool Cancer Research Organization.

The similarity between chorionic epithelial cells and carcinoma cells, and the susceptibility of the former to lead, suggested to Bell that cancer cells also might be susceptible to the effects of lead if administered in sufficient amounts.

At first metallic lead, in a finely divided state, was used intravenously in several advanced cases with some very striking results.

Routine complete examinations of blood and urine in fit patients are necessary before undertaking the treatment. In the course of this treatment, blood films are examined regularly for stippled cells and if one per field is present, treatment is usually suspended. The most important contraindications to treatment are (a) myocarditis, (b) hypertension, (c) renal impairment, (d) anemia, hemoglobin less than 50 per cent or red cells less than 3,000,000.

The preparation of lead most consistently effective is a fresh metallic suspension in gelatin. The first two doses are usually 75 mg. and then the amount is reduced to 50 mg. for the next two doses and then 25 mg. for each of the succeeding doses until 500 mg. is given. The interval between injections is usually seven to ten days but the chief guide to dosage and interval is blood examination.

The reaction to the treatment is variable, local or general or both. Usually the patient complains of pain at site of the tumor within a few hours after injection and this pain may be accompanied by swelling and edema. The general reaction affects the blood and blood forming organs with the production of anemia and stippling and there may be more or less disturbance of the gastrointestinal tract, liver, and kidney (albuminuria) and suspension of urinary output. Blue lines on the gums are rare.

Results of treatment are not startling except in isolated cases. In 227 cases treated, the percentage of success is about 20 per cent.

ADAIR-GILMAN.

Mikulicz-Radecki: Therapy of Uterine Carcinoma. Deutsche med. Wchnschr. 55: 2000, 1929.

Radiotherapy and radical surgery as therapeutic procedures for carcinoma of the cervix have been thoroughly tried out in the different German clinics and have yielded about the same result. The author believes that either technic has been developed to perfection and that further improvement of results at present will only be accomplished by a systematic combination of both therapies. In the University-Clinic of Leipzig a therapeutic plan has been adopted consisting of four consecutive steps: (1) preliminary massive radium-treatment, (2) vaginal extirpation of the uterus with subsequent radium-application, (3) postoperative series of x-ray treatment, (4) social and medical supervision for a long time after discharge from the hospital. Of course, there is a considerable number of patients on whom no operation can be performed on account of advanced carcinomatous infiltration. The preliminary radium-treatment, however, improves in some of them the local condition so much, that operation becomes feasible later on.

The carcinoma of the corpus is treated by vaginal extirpation of the uterus and removal of the adnexa. The second step is a postoperative x-ray treatment as done for cervical cancer.

G. E. GRUENFELD.

Weibel, W.: Twenty-Five Years Experience with the Wertheim Operation. Arch. f. Gynäk. 135: 1, 1928.

During the past twenty-five years the author has performed the radical Wertheim operation for carcinoma of the uterus 1500 times, 500 operations in the Bettina Hospital and 1000 in the second Frauenklinik of Vienna. In the entire series the same technic, the original procedure as outlined by Wertheim, was followed. Gradual improvement in results has not been due to improved technic but must be credited to progress in the methods of preoperative preparation, of anesthesia and of postoperative care. Of these 1500 cases, over 1000 have been followed for more than five years. From September 16, 1898, until October 18, 1922, the author saw 3184 patients suffering from carcinoma of the uterus. Of these 1515 were inoperable and 169 were treated by radiation therapy.

Weibel divides the cases into four groups: Beginning carcinoma 6.5 per cent; mild carcinoma 43 per cent; severe carcinoma 36 per cent; and very severe carcinoma 14.5 per cent. In spite of all advances in gynecology and the repeated and persistent attempts at education of the layman, there has been no improvement in either the operability or in the severity of the carcinomas at the time of operation. Patients do not present themselves any earlier for operation now than at any time previous. The operability percentages vary from year to year without any steady improvement, and range from 44 per cent to 63 per cent.

A great deal of the improvement in immediate and remote mortality is due to advance in anesthesia: 454 patients had lumbar anesthesia only, and 320 had lumbar anesthesia combined with inhalation narcosis. Weibel is definitely of the opinion that lumbar anesthesia is not only safer but also better for both the patient and the operator.

Of the postoperative complications, there were 15 per cent with injuries of the bladder, rectum or ureters, and 4 per cent had resections of the bladder, rectum or ureters; 10 per cent developed fistulas, 5 per cent had postoperative pyelitis and practically every patient developed postoperative bladder weakness or infection; 1.7 per cent had thrombosis or thrombophlebitis, 1 per cent embolism, and 12.6 per cent wound infections.

The total primary mortality was 13.8 per cent. There has been steady improvement, however, for in the first 500 operations, the primary mortality was 19 per cent, in the second 500 it was 13 per cent, and in the last 500 it dropped to 9 per cent. In beginning carcinoma the primary mortality was 8.2 per cent, in mild cases 10 per cent, in the severe types 15 per cent and in the very severe 24 per cent. Of the patients who died, 54 per cent died of peritonitis and 7.5 per cent of other infections; 6 per cent died of embolism, 0.5 per cent of ileus, 12 per cent of cardiac failure, 3 per cent of pneumonia, 8 per cent of urinary tract injury, 7 per cent of intestinal injury, 5 per cent of hemorrhage, and 3 per cent of thrombosis.

Five years following operation, 40 per cent of all operated patients were free from recurrences, or 47 per cent of those who survived the operation. Of the patients with definite secondary carcinoma of the abdominal lymph glands, 10 per cent were five year cures. Of the recurrences, 45 per cent occurred within the first year, 26 per cent within the second year, 14 per cent during the third year, 9 per cent in the fourth and 6 per cent in the fifth year.

There were in this series, 26 instances of carcinoma and pregnancy. The results obtained when pregnancy occurred were the same as for the entire group. As to age incidence, 3.5 per cent were under thirty years, and 7.2 per cent were over sixty years. There is no detectable difference in the severity of the malignancy, the operability, or the five year cures between the different decades.

RALPH A. REIS.

Schleyer, E.: The Results of the Operative Treatment of Carcinoma of the Ovary.
Monatsschr. f. Geburtsh. u. Gynäk. 79: 302, 1928.

The author analyzed all the cases of ovarian carcinoma operated upon in the First Woman's Clinic in Vienna during the years 1910 to 1925. Among 97 cases available for study the primary mortality was 12.4 per cent. Among 39 cases where the malignancy was limited to the ovaries the mortality was 2.6 per cent, whereas among 58 cases where the process had advanced beyond the confines of the ovaries the mortality was 18.9 per cent. In the 52 unilateral cases the death rate was 9.6 per cent and in the 45 bilateral cases it was 15.5 per cent.

The patients were followed up and freedom for five years was taken as the criterion for a cure. Of 57 cases available for analysis only 12 patients or 21 per cent were alive. Of the 115 cases, 102 were primary and of the 13 metastatic cases, 12 were gastrogenous in origin and one originated in the uterus.

The rule in the clinic is that unless there is a definite contraindication, every case of carcinoma of the ovary must be operated upon even if only for purposes of exploration and to make certain of the diagnosis. Both ovaries are removed because of the great frequency of recurrence if the uninvolved ovary is left behind. The uterus is removed in old women and in cases where the ovarian malignancy is metastatic because the uterus in these cases frequently contains metastases. In all other cases the uterus is removed only when there are implantation metastases on it. Rupture of a malignant cystoma during operation is a serious complication as indicated by the fact that among 13 cases where the cyst was ruptured during operation only 15.4 per cent were cured whereas among 19 unruptured cases 36.8 per cent were cured. Ascites was present in 21.7 per cent of the cases and in 83.5 per cent the menses were undisturbed.

The best prognosis is in the cases of carcinomatous degeneration of pseudomucinous cystomas and the worst prognosis in the metastatic carcinomas. Total extirpation gives the best results but cures have followed unilateral oophorectomy.

J. P. GREENHILL.

Kermauner, F.: Treatment of Carcinoma of the Uterus by Abdominal Operation.
Wien. klin. Wchnschr. 42: 1097, 1929.

This is a report of 976 cases of carcinoma of the uterus seen from 1916 to 1923 inclusive. Of them 352 were inoperable, of which about half were treated with radium or x-ray, and the rest by injections of various substances (with no improvement), or not at all. Of those treated with radium 12 or 6.4 per cent were cured for at least five years, while those treated with x-ray alone showed no cures.

The other 624 cases were operated, representing an operability of 63.9 per cent. Of these 70 or 11.2 per cent died. Five- to twelve-year cures comprise a total of 231 cases, a relative percentage of 40.4. Several of these showed recurrence after seven or eight years, and one after thirteen years. Combined radium and operation cures totaled 258 or 26.95 per cent.

The author concludes that he is not as yet ready to give up operation in favor of radium and x-ray, although he has limited operation somewhat since 1927. He stresses early recognition as being the most important factor in the determination of results.

FRANK SPIELMAN.

Peham, M.: Results with the More Extended Operative Methods in Uterine Malignancy. *Wien. klin. Wchnschr.* 42: 1622, 1929.

Operative results in uterine malignancy for the past 3 decades are compared for the purpose of determining the most efficacious operative method. The figures of Wertheim-Weibel using the more extensive abdominal methods, in their percentages

of primary mortality, and relative and absolute cures are found to be not as satisfactory as those in which the less extensive vaginal methods have been used. Illustrative of the latter are the figures of Stoeckel and the author's who use the vaginal route. The author's figures are especially significant, showing for the years 1921 to 1924 an operability of 59.7 per cent, a primary mortality of 6.9 per cent, a relative cure of 44.7 per cent, and an absolute cure of 28 per cent.

The question of wide lymph gland removal is not as important as it formerly has appeared, especially since the advent of postoperative x-ray therapy. In comparing absence of recurrence after five years, there is found to be an increase of more than 15 per cent in those free of the disease who have had x-ray, over those who have not. Besides x-ray, the difference in primary mortality also makes it advisable to use the less extensive methods.

FRANK SPIELMAN.

Schmidt, H. R.: The Operative Treatment of Operable Carcinoma of the Uterus and its Relation to Radiation Therapy. Med. Klin. 25: 623, 1929.

Since the results in cases of carcinoma of the body of the uterus are the same regardless of whether operation is performed or radium is employed, the latter should be used in technically difficult operable and inoperable cases. In cases of operable cervical cancer, however, the results of operation are not very good and the chief reason for this is the very high operative mortality. According to Heyman the average immediate death rate in 22 clinics is 17.2 per cent. The chief causes of death are cardiac weakness, hemorrhage, pneumonia, and peritonitis. The author has abandoned the preoperative roentgen-ray treatment in cases of cervical carcinoma because this must be given six weeks before operation and during this interval the patient may be lost trace of. The essential thing in securing a permanent cure is repeated radiation treatment after operation. The author employs radium ten days postoperative and repeats this ten days later. In the interval between these two radium treatments, deep x-ray therapy is given. Six months later x-ray treatment is again given. In ten cases so treated the results have been very good. Even in cases of recurrence in the vaginal scar, radium occasionally produces excellent results.

J. P. GREENHILL.

Pal, J.: The Cachexia of Malignancy and Its Control. Wien. klin. Wchnschr. 42: 321, 1929.

The efficacy of the liver treatment of pernicious anemia depends upon the ability of the bone marrow to respond to the stimulating substances found in liver which cause a regeneration of the red blood cells. This is also true in the other anemias including the cachexia of malignancy. Two of these stimulating substances have been isolated. They are amines, histamine and choline, and are found not only in liver, but also in kidney, adrenals, heart muscle, and striped muscle. Given by mouth they have produced a definite improvement in patients with inoperable carcinoma, causing an increase in weight as well as return of appetite. Adrenal extract which has a high choline content is recommended for injection. By mouth the above mentioned organs as well as their extracts can be used. Failures in their use are due to the inability of the bone marrow to respond. The influence that these substances have upon the malignancy itself has not yet been determined.

FRANK SPIELMAN.

Mandl, Felix: Prophylaxis Against Recurrence Following Operations for Malignant Tumors. Wien. klin. Wchnschr. 42: 1269, 1929.

Recurrences following operations for malignant tumors are probably the result of dissemination of malignant cells about the area excised. For this reason the author

advocates whenever possible the use of fulguration, the electric cautery, hot iron, etc. instead of the scalpel.

One of the most important factors is combating the anemia and cachexia present. Arsenic, insulin in 10 to 20 unit per day doses well controlled by carbohydrates, and liver should be used. Prophylactic postoperative x-ray therapy seems to be efficacious only in well localized malignant conditions.

FRANK SPIELMAN.

Wallart, J.: Carcinoma of the Theca Interna of a Lutein Cyst. Arch. f. Gynäk. 135: 485, 1929.

This rare tumor reported by Wallart was a carcinoma of the theca interna of a lutein cyst. The patient was forty-five years old and had a healthy child three years previously. She was operated upon for chronic appendicitis, and laparotomy disclosed a typical carcinoma developing from the theca interna. All gradations of cells were present from the small granulosa cells with dark nuclei to the lighter theca cells. The endocrine elements of the theca interna are probably of the same origin as the granulosa cells which form the greater part of the corpus luteum.

RALPH A. REIS.

Meigs, J. V.: Adenocarcinoma of the Fundus of the Uterus. New Engl. J. Med. 201: 155, 1929.

In 206 cases of body cancer seen in the Huntington Memorial Hospital, vaginal metastases were discovered in 12.1 per cent, proving that this form of metastasation is not by any means uncommon. A vaginal cancer should never be regarded as primary until the uterus has been investigated. The metastases are more likely to form by way of lymphatics or possibly venous channels than through direct implantation. If the vaginal metastases seem treatable, hysterectomy should be performed, otherwise radium is used, on the vaginal metastases preferably in form of gold or glass seeds.

EHRENFEST.

Stacy, Leda J.: Carcinoma of the Fundus of the Uterus. Surg. Gynec. Obst. 49: 43, 1929.

Although carcinoma of the fundus occurs most commonly after the menopause it is fairly common in women less than forty-five years of age, having occurred in 10.51 per cent of the cases in the series reported.

Metrorrhagia was the most common symptom and was the first symptom noted by 63.66 per cent of the patients in this series. Uterine myoma occurs more than three times as often in women with carcinoma of the fundus as in women without such carcinoma. The symptoms might be attributed to the myoma and then cause a delay in making the diagnosis of malignancy. Every patient having metrorrhagia or an abnormal vaginal discharge should be examined thoroughly to determine the cause of symptoms irrespective of age, and if the symptoms warrant it and the patient is not a poor surgical risk, hysterectomy should be done even if malignancy is not found by curettement.

The greatest number of the patients who died following operations for corpus carcinoma died during the first three years of local recurrence. More five-year arrested cases result from operation for carcinoma of the uterine fundus than from operation for carcinoma in other commonly affected organs.

WM. C. HENSKE.

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

Review of New Books

Kuntz has written a well-planned and readable book on the difficult subject of the *Autonomic Nervous System*.¹ It appears as clear cut and understandable as any description of this difficult and involved subject will allow. He uses Langley's terminology of the autonomic nervous system which covers the entire nerve supply under discussion, with further division into sympathetic and parasympathetic.

The anatomy is taken up with each individual organ discussed. Drug actions are dealt with.

The author concludes that no evidence of enervation of the ovarian follicle or of the interstitial tissue has been demonstrated, nor has any evidence of drug influence on ovarian function by nerves, been proved, although the ovarian vessels, and consequently the ovarian blood supply, is under nervous control. The uterine muscle possesses an inherent capacity to undergo rhythmic contractions. Normally the muscle is subject to both motor and inhibitory nervous control of reflex or central nervous origin.

Among the major subjects dealt with are the pathology, including neoplasms, of the autonomic system. Visceral sensitivity and referred pain are thoroughly discussed. Kuntz agrees in a limited way with the theory of vago- and sympathetico-tonia of Eppinger and Hess.

He also takes up the autonomic nervous system and its relation to the glands of internal secretion; to internal secretion; to emotion and stress; and effect of infectious diseases and cardiovascular diseases.

The concluding chapter deals with the surgery, including periarterial sympathectomy, ganglionectomy, and ramisection.

The book is an important and useful one.

—R. T. Frank.

The fourth installment of the second volume of the *Handbuch der gesamten Strahlenheilkunde, Biologie, Pathologie und Therapie*² has come to hand. The most important chapter is one dealing with radiotherapy as a means of mass treatment of carcinoma.

Lazarus observes that among civilized people on the one hand, the percentage of births is growing less, so that on the other fewer children are born but fewer die from children's diseases and plagues. As a result of this prolongation of life an increasing ballast of senile masses results. The consequence of this increase in age of the population produces an increased invalid population. In Germany in 86,000 autopsies, 10 per cent were due to death from malignant neoplasms during the years of 1920 and 1921. In England, in ten years, 40,000 women died from uterine cancers, while in Germany, 8,000 die from these yearly.

Solomon contributes a chapter on the roentgen treatment of Basedow disease; Bacmeister on the treatment of internal tuberculosis; Milani and Meldolesi on the roentgen treatment of infectious diseases.

¹The *Autonomic Nervous System*. By A. Kuntz, Ph.D., M.D., Philadelphia. 1930. Lea and Febiger.

²*Handbuch der gesamten Strahlenheilkunde, Biologie, Pathologie und Therapie*. Zweiter Band, 4. Lieferung. Herausgegeben von Prof. Dr. Paul Lazarus. J. F. Bergmann, München. 1930.

Béclère and Levy discuss the radiotherapeutic treatment of the nervous system which not only includes tumors, but also such diseases as syringomyelia, multiple sclerosis, tabes, and poliomyelitis, as well as peripheral nervous trouble. The concluding chapter is by Czerny and Karger on radiotherapy of children's diseases, in which, naturally, sunlight and ultraviolet therapy also play a large rôle.

—R. T. Frank.

In this amusing little booklet, *Expectant Fathers*,⁴ the author defends his plea that expectant fathers are entitled to some consideration on the part of attending obstetricians and especially maternity hospitals, in view of the lavish attention commonly bestowed on the expectant mother. No doubt, something ought to be done for them. His suggestion for a Bulletin Board announcing from time to time the progress the wife is making is not so bad. He seems particularly impressed with twilight sleep and one cannot escape the feeling that with greater benefit, at least for the attending obstetrician, twilight should be administered to the waiting husband—after all what difference would it make if he were a bit blue after it is all over? However, we agree with the advice on the blurb—this book should be kept in the doctor's waiting room and several copies in the anterooms of maternity wards.

—Dr. Hugo Ehrenfest.

Dr. Crossen's *Diseases of Women*⁵ has become a classic in gynecologic literature. The logical arrangement of the topics, the thoroughness of illustration and the lucidity and conciseness of discussion combine to produce a volume of unusual worth.

This present book fully maintains the standards set by the former editions. The name of Dr. R. J. Crossen appears for the first time as a co-author, and his revision of the section on sterility gives a most complete discussion, theoretical and clinical, with full reference to many of the most recent suggestions regarding this often baffling condition. It is of interest to note a section on therapeutic contraception.

Dr. Hugo Ehrenfest has brought the chapter on the Internal Secretory Glands in Relation to Gynecology quite up-to-date with a review of the newer conception of the physiology of menstruation based upon the work of Aschheim and Zondek, Frank, Allen and Doisy, and Smith and Engle. We can hope with the author for the early offering of a pure and standardized anterior pituitary hormone in order that organo-therapy may be put on a scientific and rational basis.

Dr. H. S. Brookes, Jr., is responsible for a new chapter on the Lower Intestinal Tract in Relation to Gynecology. It is surprising how much practical information, diagnosis, and treatment has been packed in these twenty pages.

It is apparent that the gynecologic literature of the past few years has been closely scrutinized and few, if any, true advances or suggestions of real merit will be found to have been omitted in this revision.

—Philip F. Williams.

⁴*Expectant Fathers. Their Care and Treatment.* By Douglas V. Martin. Illustrated. St. Louis, 1930. De Vass Publishing Co., Wainwright Building.

⁵*Diseases of Women.* By Harry Sturgeon Crossen and Robert James Crossen. 7th ed., St. Louis, 1930. The C. V. Mosby Company.